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(54) Title: SUBSTITUTED AMIDE DERIVATIVES AS PROTEIN KINASE INHIBITORS

(57) Abstract: Selected compounds are effective for prophylaxis and treatment of diseases, such as HGF mediated diseases. The invention encompasses novel compounds, analogs, prodrugs and pharmaceutically acceptable salts thereof, pharmaceutical compositions and methods for prophylaxis and treatment of diseases and other maladies or conditions involving, cancer and the like. The subject invention also relates to processes for making such compounds as well as to intermediates useful in such processes.

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SUBSTITUTED AMIDE DERIVATIVES AS PROTEIN KINASE INHIBITORS

FIELD OF THE INVENTION

This invention is in the field of pharmaceutical agents and specifically relates to compounds, compositions, uses and methods for treating cancer.

BACKGROUND OF THE INVENTION

Protein kinases represent a large family of proteins, which play a central role in the regulation of a wide variety of cellular processes, maintaining control over cellular function. A partial list of such kinases includes abl, Akt, bcr-abl, Blk, Brk, Btk, c-kit, c-Met, c-src, c-fms, CDK1, CDK2, CDK3, CDK4, CDK5, CDK6, CDK7, CDK8, CDK9, CDK10, cRaf1, CSF1R, CSK, EGFR, ErbB2, ErbB3, ErbB4, Erk, Fak, fes, FGFR1, FGFR2, FGFR3, FGFR4, FGFR5, Fgr, flt-1, Fps, Frk, Fyn, Hck, IGF-1R, INS-R, Jak, KDR, Lck, Lyn, MEK, p38, PDGFR, PIK, PKC, PYK2, ros, tie, tie2, TRK, Yes, and Zap70. Inhibition of such kinases has become an important therapeutic target.

Certain diseases are known to be associated with deregulated angiogenesis, for example ocular neovascularisation, such as retinopathies (including diabetic retinopathy), age-related macular degeneration, psoriasis, hemangioblastoma, hemangioma, arteriosclerosis, inflammatory disease, such as a rheumatoid or rheumatic inflammatory disease, especially arthritis (including rheumatoid arthritis), or other chronic inflammatory disorders, such as chronic asthma, arterial or post-transplantational atherosclerosis, endometriosis, and neoplastic diseases, for example so-called solid tumors and liquid tumors (such as leukemias).

At the center of the network regulating the growth and differentiation of the vascular system and its components, both during embryonic development and normal growth, and in a wide number of pathological anomalies and diseases, lies the angiogenic factor known as Vascular Endothelial Growth Factor"(VEGF; originally termed 'Vascular Permeability Factor", VPF), along with its cellular receptors (see G. Breier et al., Trends in Cell Biology, 6:454-456 (1996)).

VEGF is a dimeric, disulfide-linked 46-kDa glycoprotein related to "Platelet-Derived Growth Factor" (PDGF); it is produced by normal cell lines and tumor cell lines; is an endothelial cell-specific mitogen; shows angiogenic activity in in vivo test systems (e.g. rabbit cornea); is chemotactic for endothelial cells and monocytes; and induces plasminogen activators in endothelial cells, which are involved in the proteolytic degradation of extracellular matrix during the formation of capillaries. A number of isoforms of VEGF are known, which show comparable biological activity, but differ in the type of cells that secrete

them and in their heparin-binding capacity. In addition, there are other members of the VEGF family, such as "Placenta Growth Factor"(PlGF) and VEGF-C.

VEGF receptors (VEGFR) are transmembranous receptor tyrosine kinases. They are characterized by an extracellular domain with seven immunoglobulin-like domains and an intracellular tyrosine kinase domain. Various types of VEGF receptor are known, e.g. VEGFR-1 (also known as flt-1), VEGFR-2 (also known as KDR), and VEGFR-3.

A large number of human tumors, especially gliomas and carcinomas, express high levels of VEGF and its receptors. This has led to the hypothesis that the VEGF released by tumor cells stimulates the growth of blood capillaries and the proliferation of tumor endothelium in a paracrine manner and through the improved blood supply, accelerates tumor growth. Increased VEGF expression could explain the occurrence of cerebral edema in patients with glioma. Direct evidence of the role of VEGF as a tumor angiogenesis factor in vivo is shown in studies in which VEGF expression or VEGF activity was inhibited. This was achieved with anti-VEGF antibodies, with dominant-negative VEGFR-2 mutants, which inhibited signal transduction, and with antisense-VEGF RNA techniques. All approaches led to a reduction in the growth of glioma cell lines or other tumor cell lines in vivo as a result of inhibited tumor angiogenesis.

Angiogenesis is regarded as an absolute prerequisite for tumors, which grow beyond a diameter of about 1-2 mm; up to this limit, oxygen and nutrients may be supplied to the tumor cells by diffusion. Every tumor, regardless of its origin and its cause, is thus dependent on angiogenesis for its growth after it has reached a certain size.

Three principal mechanisms play an important part in the activity of angiogenesis inhibitors against tumors: 1) Inhibition of the growth of vessels, especially capillaries, into avascular resting tumors, with the result that there is no net tumor growth owing to the balance that is achieved between cell death and proliferation; 2) Prevention of the migration of tumor cells owing to the absence of blood flow to and from tumors; and 3) Inhibition of endothelial cell proliferation, thus avoiding the paracrine growth-stimulating effect exerted on the surrounding tissue by the endothelial cells which normally line the vessels. See R. Connell and J. Beebe, Exp. Opin. Ther. Patents, 11:77-114 (2001).

VEGF's are unique in that they are the only angiogenic growth factors known to contribute to vascular hyperpermeability and the formation of edema. Indeed, vascular hyperpermeability and edema that is associated with the expression or administration of many other growth factors appears to be mediated via VEGF production.

Inflammatory cytokines stimulate VEGF production. Hypoxia results in a marked upregulation of VEGF in numerous tissues, hence situations involving infarct, occlusion, ischemia, anemia, or circulatory impairment typically invoke VEGF/VPF-mediated responses. Vascular hyperpermeability, associated edema, altered transendothelial exchange and macromolecular extravasation, which is often accompanied by diapedesis, can result in excessive matrix deposition, aberrant stromal proliferation, fibrosis, etc. Hence, VEGF-mediated hyperpermeability can significantly contribute to disorders with these etiologic features. As such, regulators of angiogenesis have become an important therapeutic target.

The hepatocyte growth factor receptor ("c-Met") is a unique receptor tyrosine kinase shown to be overexpressed in a variety of malignancies. c-Met typically comprises, in its native form, a 190-kDa heterodimeric (a disulfide-linked 50-kDa α-chain and a 145-kDa β-chain) membrane-spanning tyrosine kinase protein (Proc. Natl. Acad. Sci. USA, 84:6379-6383 (1987)). c-Met is mainly expressed in epithelial cells and stimulation of c-Met leads to scattering, angiogenesis, proliferation and metastasis. (See Cytokine and Growth Factor Reviews, 13:41-59 (2002)).

The ligand for c-Met is hepatocyte growth factor (also known as scatter factor, HGF and SF). HGF is a heterodimeric protein secreted by cells of mesodermal origin (Nature, 327:239-242 (1987); J. Cell Biol., 111:2097-2108 (1990)).

Various biological activities have been described for HGF through interaction with c-met (Hepatocyte Growth Factor- Scatter Factor (HGF-SF) and the c-Met Receptor, Goldberg and Rosen, eds., Birkhauser Verlag-Basel, 67-79 (1993). The biological effect of HGF/SF may depend in part on the target cell. HGF induces a spectrum of biological activities in epithelial cells, including mitogenesis, stimulation of cell motility and promotion of matrix invasion (Biochem. Biophys. Res. Comm., 122:1450-1459 (1984); Proc. Natl. Acad. Sci. U.S.A., 88:415-419 (1991)). It stimulates the motility and invasiveness of carcinoma cells, the former having been implicated in the migration of cells required for metastasis. HGF can also act as a "scatter factor", an activity that promotes the dissociation of epithelial and vascular endothelial cells (Nature, 327:239-242 (1987); J. Cell Biol., 111:2097-2108 (1990); EMBO J., 10:2867-2878 (1991); Proc. Natl. Acad. Sci. USA, 90:649-653 (1993)). Therefore, HGF is thought to be important in tumor invasion (Hepatocyte Growth Factor-Scatter Factor (HGF-SF) and the C-Met Receptor, Goldberg and Rosen, eds., Birkhauser Verlag-Basel, 131-165 (1993)).

HGF and c-Met are expressed at abnormally high levels in a large variety of solid tumors. High levels of HGF and/or c-Met have been observed in liver, breast, pancreas, lung, kidney, bladder, ovary, brain, prostate, gallbladder and myeloma tumors in addition to many

others. The role of HGF/c-Met in metastasis has been investigated in mice using cell lines transformed with HGF/c-Met (J. Mol. Med., 74:505-513 (1996)). Overexpression of the c-Met oncogene has also been suggested to play a role in the pathogenesis and progression of thyroid tumors derived from follicular epithelium (Oncogene, 7:2549-2553 (1992)). HGF is a morphogen (Development, 110:1271-1284 (1990); Cell, 66:697-711 (1991)) and a potent angiogenic factor (J. Cell Biol., 119:629-641 (1992)).

Recent work on the relationship between inhibition of angiogenesis and the suppression or reversion of tumor progression shows great promise in the treatment of cancer (Nature, 390:404-407 (1997)), especially the use of multiple angiogenesis inhibitors compared to the effect of a single inhibitor. Angiogenesis can be stimulated by HGF, as well as vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF).

Angiogenesis, the process of sprouting new blood vessels from existing vasculature and arteriogenesis, the remodeling of small vessels into larger conduit vessels are both physiologically important aspects of vascular growth in adult tissues. These processes of vascular growth are required for beneficial processes such as tissue repair, wound healing, recovery from tissue ischemia and menstrual cycling. They are also required for the development of pathological conditions such as the growth of neoplasias, diabetic retinopathy, rheumatoid arthritis, psoriasis, certain forms of macular degeneration, and certain inflammatory pathologies. The inhibition of vascular growth in these contexts has also shown beneficial effects in preclinical animal models. For example, inhibition of angiogenesis by blocking vascular endothelial growth factor or its receptor has resulted in inhibition of tumor growth and in retinopathy. Also, the development of pathological pannus tissue in rheumatoid arthritis involves angiogenesis and might be blocked by inhibitors of angiogenesis.

The ability to stimulate vascular growth has potential utility for treatment of ischemia-induced pathologies such as myocardial infarction, coronary artery disease, peripheral vascular disease, and stroke. The sprouting of new vessels and/or the expansion of small vessels in ischemic tissues prevents ischemic tissue death and induces tissue repair. Certain diseases are known to be associated with deregulated angiogenesis, for example ocular neovascularization, such as retinopathies (including diabetic retinopathy), age-related macular degeneration, psoriasis, hemangioblastoma, hemangioma, arteriosclerosis, inflammatory disease, such as a rheumatoid or rheumatic inflammatory disease, especially arthritis (including rheumatoid arthritis), or other chronic inflammatory disorders, such as chronic asthma, arterial or post-transplantational atherosclerosis, endometriosis, and neoplastic diseases, for example so-called

solid tumors and liquid tumors (such as leukemias). Treatment of malaria and related viral diseases may also be mediated by HGF and cMet.

Elevated levels of HGF and c-Met have also been observed in non-oncological settings, such as hypertension, myocardial infarction and rheumatoid arthritis. It has been observed that levels of HGF increase in the plasma of patients with hepatic failure (Gohda et al., supra) and in the plasma (Hepatol., 13:734-750 (1991)) or serum (J. Biochem., 109:8-13 (1991)) of animals with experimentally induced liver damage. HGF has also been shown to be a mitogen for certain cell types, including melanocytes, renal tubular cells, keratinocytes, certain endothelial cells and cells of epithelial origin (Biochem. Biophys. Res. Commun., 176:45-51 (1991); Biochem. Biophys. Res. Commun., 174:831-838 (1991); Biochem., 30:9768-9780 (1991); Proc. Natl. Acad. Sci. USA, 88:415-419 (1991)). Both HGF and the c-Met proto-oncogene have been postulated to play a role in microglial reactions to CNS injuries (Oncogene, 8:219-222 (1993)).

Metastatic SCC cells overexpress c-Met and have enhanced tumoregenesis and metastasis in vivo [G. Gong et al., Oncogene, 23:6199-6208 (2004)]. C-Met is required for tumor cell survival [N. Shinomiya et al., Cancer Research, 64:7962-7970 (2004)]. For a general review see C. Birchmeier et al., Nature Reviews/Molecular Biology 4:915-925 (2003).

In view of the role of HGF and/or c-Met in potentiating or promoting such diseases or pathological conditions, it would be useful to have a means of substantially reducing or inhibiting one or more of the biological effects of HGF and its receptor. Thus a compound that reduces the effect of HGF would be a useful compound. Compounds of the current invention have not been previously described as inhibitors of angiogenesis such as for the treatment of cancer.

Kirin Japanese patent application JP11158149, published 28 November 1997, describes substituted phenyl compounds. Kirin publication WO 00/43366 describes substituted phenyl compounds. Kirin publication WO 03/000660 describes substituted phenyl compounds. Substituted quinolines are described in US Patent No. 6,143,764. WO 02/32872 describes substituted quinolines. Patent Application WO 00/47212 describes substituted quinazoline derivatives. Patent Application WO 98/37079 describes substituted N-heterocyclic compounds. Kubo et al, Biorg. Med. Chem., 11:5117-33 (2003) describes phenoxyquinoline derivatives. Patent Application WO 04/46133, published 3 June 2004, describes amino-heterocycles for treating pain. Patent Application WO 03/004472, published 16 January 2003, describes pyrazine-2-carboxamides. JP63145272, published 17 June 1988, describes 4,5-dihydro-6-(4-substituted phenyl)-3(2H)-pyridazinones. Kamel, et al., Egyptian J. of Pharm.

Sci., 38:61-69 (1997) describes 4-substituted phenoxyquinolines. Patent Application WO 04/18430, published 4 March 2004, describes quinoline derivatives. Patent Application WO 02/32872, published 25 April 2002, describes urea derivatives. Patent Application WO 04/37784, published 6 May 2004, describes substituted pyrrolidones. Patent Application WO 00/50405 published 31 August 2000, describes quinoline-6-carboxamides. Patent Application WO 04/083235, published 30 September 2004, describes azaheterocyclyl aromatic compounds.

Compounds of the current invention have not been described as inhibitors of c-Met such as for the treatment of cancer.

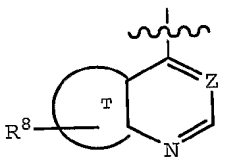
DESCRIPTION OF THE INVENTION

A class of compounds useful in treating cancer and angiogenesis is defined by Formula I

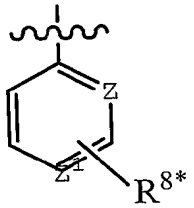
R-X-W-Y-R^1 **I**

enantiomers, diastereomers, salts solvates, and N-oxides thereof wherein

R is



; or



T is selected from phenyl, 5-6-membered heteroaryl, or 5-6 membered heterocyclyl;

Z is selected from N or CR^7;

Z^1 is selected from N or CR^7;

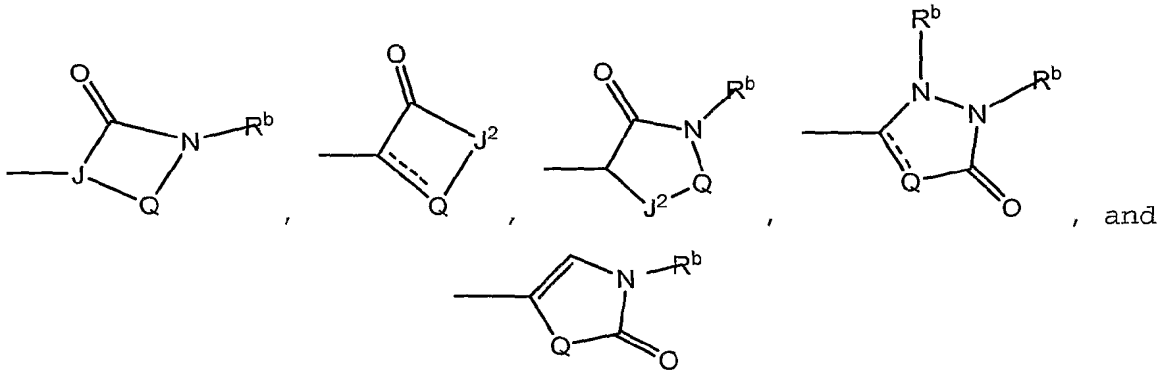
W is a substituted or unsubstituted phenyl, a substituted or unsubstituted benzomorpholinyl, a substituted or unsubstituted 6-membered nitrogen containing heteroaryl; a substituted or unsubstituted c_{3-7}cycloalkyl, c_{1-6}alky and c_{1-6}alkynyl;

X is selected from O, S, S(=O), SO_2, NR^2 and CR^3R^4;

Y is selected from $-NR^aC(=O)-(CR^3R^4)_p-$, $-NR^aC(=S)-(CR^3R^4)_p-$, $-NR^a-(CR^3R^4)_p-$, $-NR^a-(CR^3R^4)_pC(=O)-$, $-NR^a-(CR^3R^4)_pC(=S)-$, $-NR^aS(=O)_t-$, $-NR^aS(=O)_t-(CR^3R^4)_p-$, $-C(=O)NR^a-(CR^3R^4)_p-$, and $-NR^a-(CR^3R^4)_p-S(=O)_t-$, and where W is benzomorpholinyl Y may further include -C(=O);

R^a is selected from H, alkyl, heterocyclyl, aryl, arylalkyl, heterocyclylalkyl, cycloalkyl, cycloalkylalkyl, alkenyl and alkynyl; wherein R^a is optionally substituted;

R^1 is a partially unsaturated or saturated ring selected from



wherein J is N or CR^{4a};

J^2 is O or $CR^{4a}R^{4a}$;

Q is a 1-5 membered saturated or partially unsaturated alkly chain, or a 2-5 membered saturated or partially unsaturated heteroalkyl chain;

R^1 is optionally fused with an optionally substituted phenyl or an optionally substituted 5-6 membered heterocyclyl ring;

wherein R^1 is optionally substituted with one or more substituents independently selected from H, halo, hydroxyl, $R^{5a}R^aN$-, $R^{5a}R^aN$-C_{1-6} alkyl, $R^5(S=O)$-C_{1-6} alky, NR^5R^{5a}-$(C=O)$-C_{1-6} alky, optionally substituted alkyl, alkenyl hydroxyalkyl, C_{1-6} alkoxy-C_{1-6} alkyl, alkenylalkyl, C_{1-6} alkylthio-C_{1-3} alkyl, -C_{1-6} alkyl-NR^a-$C(=O)$-OR^5, -C_{1-3} alkyl-NR^a-$(C=O)$-R^5, -C_{1-3} alkyl-$C(=O)$- C_{1-3} alkyl, aminoalkyl, hydroxy-substituted aminoalkyl, hydroxy-substituted haloalkyl, (heterocyclo)hydroxyalkyl, haloC_{1-6}-alkyl, azidoalkyl, optionally substituted aryl-C_{1-6} alkyl, optionally substituted 5-6-membered heterocyclyl-C_{1-6} alkyl, optionally substituted C_{1-6}-alkyl, optionally substituted C_{3-7} cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted 5-10 membered heteroaryl, optionally, optionally substituted C_{3-6} cycloalkyl, substituted heteroarylalkyl, optionally substituted arylalkyl, and optionally substituted C_{6-10} aryl;

R^2 is selected from H, alkyl, haloalkyl, aryl, heterocyclyl, arylalkyl, heterocyclylalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl and R^5-carbonyl;

R^3 and R^4 are each independently selected from H, alkyl, aryl, heterocyclyl, arylalkyl, heterocyclylalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, R^6 and alkyl substituted with R^6; alternatively R^3 and R^4, together with the carbon atom they are attached to, form an optionally substituted 3-6 membered ring;

R^{3a} is absent or is selected from H, alkyl, aryl, heterocyclyl, arylalkyl, heterocyclylalkyl, cycloalkyl, cycloalkylalkyl, R^6 and alkyl substituted with R^6;

R^{4a} is absent or is selected from H, halo, $-OR^5$ $-NR^aR^5$, alkyl, aryl, heterocyclyl, arylalkyl, heterocyclylalkyl, cycloalkyl, cycloalkylalkyl, R^6 and alkyl substituted with R^6;

R^5 is independently selected at each occurrence from H, alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, alkylaminoalkyl, alkylthioalkyl, arylalkyl, heterocyclylalkyl, cycloalkylalkyl, aryl, heterocyclyl, alkenyl, alkynyl and cycloalkyl;

R^{5a} is independently selected at each occurrence from H, alkyl, haloalkyl, arylalkyl aminoalkyl, heterocyclylalkyl, cycloalkylalkyl, aryl, heterocyclyl, alkenyl, alkynyl and cycloalkyl;

or when R^5 and R^a, or $R^{5a}$and R^a is bonded to the same nitrogen atom, R^a and R^5, or R^a and R^{5a} may independently optionally combine to form a heterocyclo ring.

R^6 is selected from cyano, $-OR^2$, $-SR^2$, halo, $-SO_2R^2$, $-C(=O)R^2$, $-SO_2NR^2R^5$, $-NR^5C(=O)OR^2$, $-NR^5C(=O)NR^5R^2$, $-NR^5C(=O)R^2$, $-CO_2R^2$, $-C(=O)NR^2R^5$ and $-NR^2R^5$;

R^7 is selected from H, halo, cyano, $-C(=O)NR^aR^5$ and alkyl;

R^8 is one or more substituents independently selected at each occurrence from H, cyano, hydroxyl, halo, optionally substituted heterocyclyl, $-C(=O)NR^aR^5$, $-OC(=O)NR^aR^5$, $-NR^aC(=O)OR^5$, $-NR^aC(=O)-R^5$, $R^5R^aN-O_2S-$, R^5O_2S-, $R^5O_2SR^aN-$, R^5R^aN-, alkyl, aminoalkyl, alkylaminoalkyl, alkoxyalkyl, phenylalkyl, heterocyclylalkyl, alkoxy, haloalkoxy, alkylaminoalkoxy, arylalkoxy, heterocyclylalkoxy, cycloalkylalkoxy, heterocyclyl(hydroxyalkoxy), cycloalkyl(hydroxyalkoxy), aryl(hydroxyalkoxy), alkoxyalkoxy, aryloxyalkoxy, heterocyclyloxyalkoxy, cycloalkyloxyalkoxy, aryloxy, heterocyclyloxy, cycloalkyloxy; aryl and heteroaryl, alternatively where R^8 comprises an NR^aR^5 moiety R^a and R^5, together with the nitrogen atom they are attached to, may optionally form a substituted or unsubstituted 4-6 membered ring;

R^{8*} is one or more substituents independently selected at each occurrence from H, cyano, hydroxyl, halo, optionally substituted heterocyclyl, $-NR^aC(=O)NR^aR^5$, $NR^aC(=NR^b)-NR^5$, $NR^aC(=S)NR^aR^5$, $-OC(=O)NR^aR^5$, $-NR^aC(=O)OR^5$, $-NR^aC(=O)-R^5$, $R^5R^aN-O_2S-$, R^5O_2S-, $R^5O_2SR^aN-$, R^5R^aN-, alkyl, aminoalkyl, alkylaminoalkyl, alkoxyalkyl, phenylalkyl, heterocyclylalkyl, alkoxy, haloalkoxy, alkylaminoalkoxy, arylalkoxy, heterocyclylalkoxy, cycloalkylalkoxy, heterocyclyl(hydroxyalkoxy), cycloalkyl(hydroxyalkoxy), aryl(hydroxyalkoxy), alkoxyalkoxy, aryloxyalkoxy, heterocyclyloxyalkoxy, cycloalkyloxyalkoxy, aryloxy, heterocyclyloxy, and cycloalkyloxy; alternatively where R^{8a} comprises an NR^aR^5 moiety R^a and R^5, together with the nitrogen atom they are attached to, may optionally form a substituted or unsubstituted 4-6 membered ring;

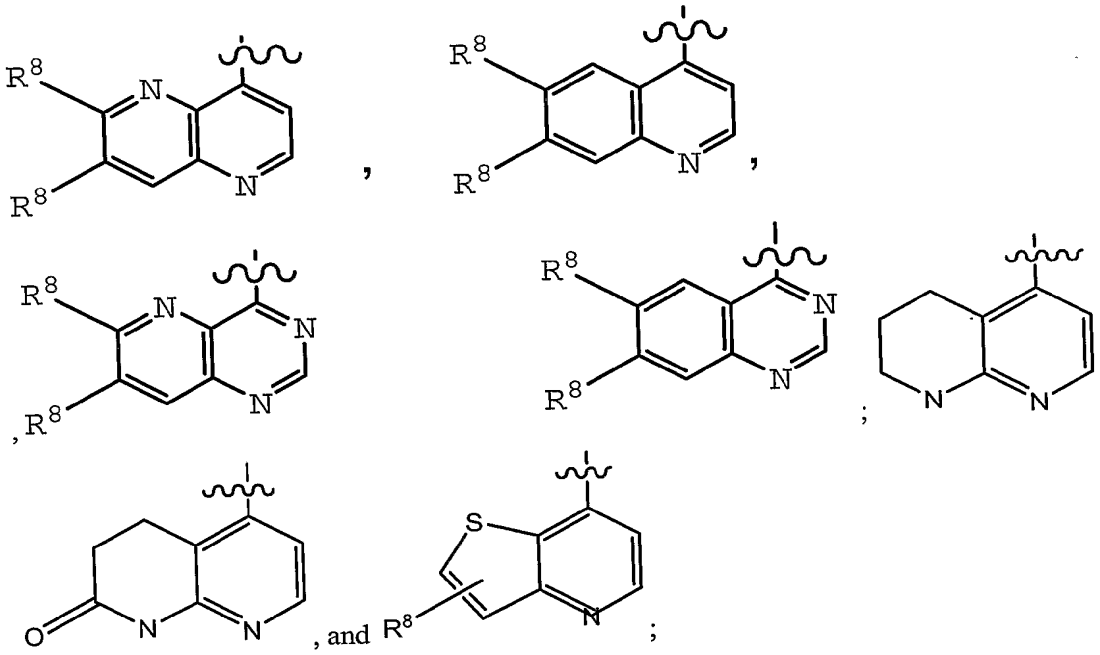
p is 0, 1, 2, or 3; and

t is 0, 1 or 2;

wherein each alkyl, aryl, heteroaryl, cycloalkyl, alkenyl, alkynyl, heterocyclyl, and alkoxy moiety of any R, R^1, R^2, R^3, R^4, R^5, R^7, R^8, R^{8*}, and R^a is optionally independently substituted with one or more groups independently selected at each occurrence from halo, oxo, $-NR^aR^5$, $-OR^{5a}$, $-CO_2R^5$, $-C(=O)R^5$, $(C_1\text{-}C_6)$alkylamino, -NH-N=NH, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkynyl, $(C_3\text{-}C_6)$cycloalkyl, $(C_1\text{-}C_6)$haloalkyl, di$(C_1\text{-}C_6)$alkylamino, $(C_1\text{-}C_6)$alkylamino-$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$hydroxyalkylamino, $(C_1\text{-}C_6)$alkylamino-$(C_1\text{-}C_6)$alkylamino, phenyl, heterocyclic, heteroaryl, $-(CR^3R^4)_p$alkyl-S(=O)-alkyl, and $-(CR^3R^4)_p$alkyl-$S(O)_2$-alkyl.

The invention also relates to compounds wherein

R is selected from



; and ;

R^8 is independently selected from H, cyano, hydroxy, $-C(=O)NR^aR^{5a}$, 5-6 membered heterocyclyl, $-NR^aC(=O)-R^{5a}$, $R^{5a}R^aN\text{-}O_2S\text{-}$, $R^{5a}O_2SR^aN\text{-}$, $R^{5a}R^aN\text{-}$, $C_{1\text{-}6}$-alkyl, amino-$C_{1\text{-}6}$-alkyl, $C_{1\text{-}6}$-alkylamino-$C_{1\text{-}6}$-alkyl, alkoxy-$C_{1\text{-}6}$-alkyl, phenyl-$C_{1\text{-}6}$-alkyl, heterocyclyl-$C_{1\text{-}6}$-alkyl, $C_{1\text{-}6}$-alkoxy, halo-$C_{1\text{-}6}$-alkoxy, $C_{1\text{-}6}$-alkylamino-$C_{1\text{-}6}$-alkoxy, aryl-$C_{1\text{-}6}$-alkoxy, 5-6-membered heterocyclyl-$C_{1\text{-}6}$-alkoxy, $C_{3\text{-}6}$-cycloalkyl-$C_{1\text{-}6}$-alkoxy, 5-6-membered heterocyclyl(hydroxyl-$C_{1\text{-}6}$-alkoxy), $C_{3\text{-}6}$-cycloalkyl(hydroxyl-$C_{1\text{-}6}$-alkoxy), phenyl(hydroxyl-$C_{1\text{-}6}$-alkoxy), $C_{1\text{-}6}$-alkoxy-$C_{1\text{-}6}$-alkoxy, phenyloxy-$C_{1\text{-}6}$-alkoxy, 5-6

membered heterocyclyloxy-C_{1-6}-alkoxy, C_{3-6}-cycloalkyloxy-C_{1-6}-alkoxy, phenyloxy, 5-6-membered heterocyclyloxy, and C_{3-6}-cycloalkyloxy;

R^a is selected from H, C_{1-6}-alkyl, 5-6 membered heterocyclyl, phenyl, phenyl-C_{1-6}-alkyl, 5-6 membered heterocyclyl-C_{1-6}-alkyl, C_{3-6}-cycloalkyl, C_{3-6}-cycloalkyl-C_{1-6}-alkyl, C_{2-6}-alkenyl and C_{2-6}-alkynyl; and

R^{5a} is selected from H, C_{1-6}-alkyl, C_{1-6}-haloalkyl, phenyl-C_{1-6}-alkyl, 5-6 membered heterocyclyl-C_{1-6}-alkyl, C_{3-6}-cycloalkyl-C_{1-6}-alkyl, phenyl, 5-6-membered heterocyclyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl and C_{3-6}-cycloalkyl;

in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

R^8 is independently selected from H, cyano, aminocarbonyl, C_{1-3}-alkylaminocarbonyl, C_{1-6}-alkyl, C_{1-6}-alkoxy, C_{1-3}-alkylamino-C_{1-3}-alkoxy, 5-6 membered heterocyclyl-C_{1-3}-alkoxy, C_{4-6}-cycloalkyl-C_{1-3}-alkoxy, 5-6 membered heterocyclyl-C_{1-3}-(hydroxyalkoxy), C_{3-6}-cycloalkyl-C_{1-3}-(hydroxyalkoxy), C_{1-2}-alkoxy-C_{1-3}-alkoxy, phenyloxy-C_{1-3}alkoxy, 5-6 membered heterocyclyloxy-C_{1-3}-alkoxy, cycloalkyloxy-C_{1-3}-alkoxy, 5-6 membered heterocyclyloxy, and C_{3-6}-cycloalkyloxy; in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

R^8 is independently selected from H, methyl, cyano, aminocarbonyl, methylaminocarbonyl, methoxy, dimethylaminopropoxy, 3-(morpholin-4-yl)ethoxy, 3-(pyrrolidin-1-yl)propoxy, 2-hydroxy-3-(morpholin-4-yl)propoxy, 3-(1,2,4-triazol-1-yl)propoxy, 3-(4-methylpiperazin-1-yl)propoxy, 3-(piperidin-4-yl)propoxy, dimethylaminoethoxy and diethylaminoethoxy; in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

R is selected from 6,7-dimethoxy-4-quinolinyl, 6-methoxy-7-(dimethylaminopropoxy)-4-quinolinyl, 6-methoxy-7-(3-(morpholin-4-yl)propoxy)-4-quinolinyl, 6-methoxy-7-(3-(pyrrolidin-1-yl)propoxy)-4-quinolinyl, 6-methoxy-7-(2-hydroxy-3-(morpholin-4-yl)propoxy)-4-quinolinyl, 6-methoxy-7-(3-(1,2,4-triazol-1-yl)propoxy)-4-quinolinyl, 6-methoxy-7-(3-(4-methylpiperazin-1-yl)propoxy)-4-quinolinyl, 6-methoxy-7-(3-(piperidin-4-yl)propoxy)-4-quinolinyl, 6,7-dimethoxy-4-quinazolinyl and 6-methoxy-7-(dimethylaminopropoxy)-4-quinazolinyl; in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

W is selected from substituted or unsubstituted phenyl, substituted or unsubstituted pyridyl, substituted or unsubstituted pyrimidinyl, substituted or unsubstituted pyridazinyl and substituted or unsubstituted pyrazinyl; in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

W is substituted or unsubstituted phenyl; in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

W is substituted or unsubstituted pyridyl; in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

X is O; in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

Y is selected from -NHC(=O)-, –NHC(=O)-$(CH_2)_p$-, –NH-$(CH_2)_p$-, and –NH-$(CH_2)_p$C(=O)-; and wherein

p is 0 or 1; in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

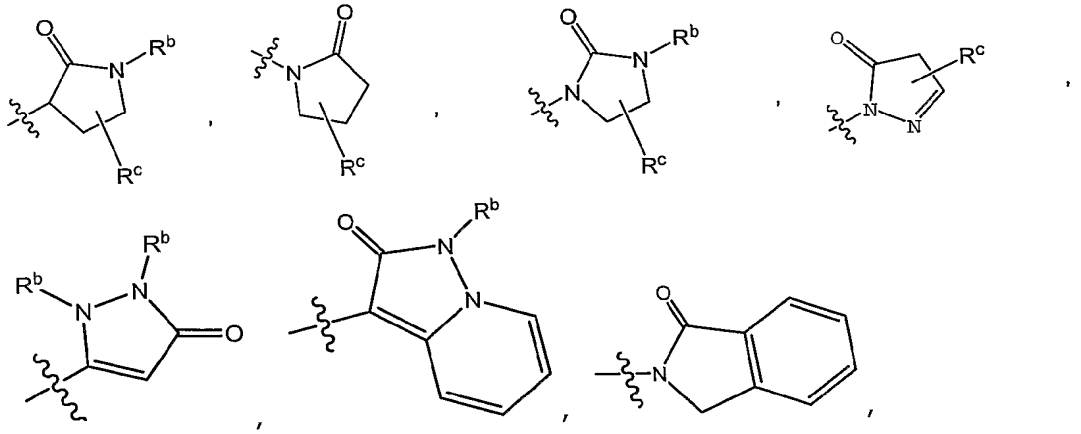
Y is -NHC(=O)-; in conjunction with any of the above or below embodiments.

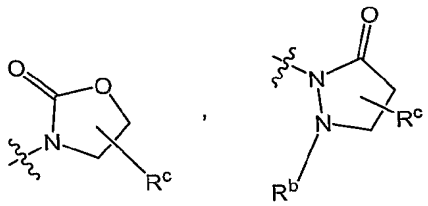
The invention also relates to compounds wherein

p is 1; in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

R^1 is selected from





R^b is independently selected at each occurrence from H, optionally substituted arylalkyl, optionally substituted 5-6-membered heterocyclyl-C_{1-3} alkyl, optionally substituted C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted C_{6-10} ary, optionally substituted C_{6-10} heteroaryl, optionally substituted C_{3-6} cycloalkyl, and $R^aR^{5a}N$-C_{1-3}alkyl;

R^c is one or more substituents selected from H, methyl, isopropyl, tert-butyl, bromo, fluoro, hydroxyl, $R^{5a}R^aN$-, $R^{5a}R^aN$-C_{1-3} alkyl, methoxymethyl, methoxyethyl, methylthiomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, optionally substituted phenyl, optionally substituted pyridyl, optionally substituted thienyl, and optionally substituted benzyl; wherein R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; C_{6-10} aryl, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, $-C(=O)R^{5a}$ and optionally substituted heteroraryl

R^a is selected from H, C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, optionally substituted phenyl-C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl-C_{1-6}-alkyl, C_{3-6}-cycloalkyl, C_{3-6}-cycloalkyl-C_{1-6}-alkyl, C_{2-6}-alkenyl and C_{2-6}-alkynyl; and

R^{5a} is selected from H, C_{1-6}-alkyl, C_{1-6}-haloalkyl, phenyl-C_{1-6}-alkyl, 5-6 membered heterocyclyl-C_{1-6}-alkyl, C_{3-6}-cycloalkyl-C_{1-6}-alkyl, $R^aC(=O)$-, optionally substituted phenyl, optionally substituted 5-6-membered heterocyclyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl and C_{3-6}-cycloalkyl; or wherein

two adjacent R^c substituents, two adjacent R^b substituents or R^c together with an adjacent R^b together form an optionally substituted fused ring; or wherein

two R^c substituents, together form an optionally substituted spiro ring; in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

R^b is selected from H, optionally substituted benzyl, C_{1-3} alkylaryl, C_{1-3} alkylheteroaryl, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, methoxymethyl,, -(C_{1-6})alkyl,2-hydroxy 2-methylbutyl, 2-hydroxy-2-methylpropyl, 2-hydroxypropyl, 1-(1-hydroxycyclopropyl)methyl,, ethylaminomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, pyridyl, thienyl, optionally substituted phenyl,1-naphthy, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, and $-C(=O)R^{5a}$;

R^c is one or more substituents selected from H, methyl, isopropyl, tert-butyl, bromo, fluoro, hydroxyl, $R^{5a}R^aN$-, $R^{5a}R^aN$-C_{1-3} alkyl, methoxymethyl, methoxyethyl, methylthiomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, optionally substituted phenyl, optionally substituted pyridyl, optionally substituted thienyl, and optionally substituted benzyl; wherein R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; C_{6-10} aryl, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, $-C(=O)R^{5a}$ and optionally substituted heteroraryl

wherein

R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; C_{6-10} aryl, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, $-C(=O)R^{5a}$ and optionally substituted heteroraryl

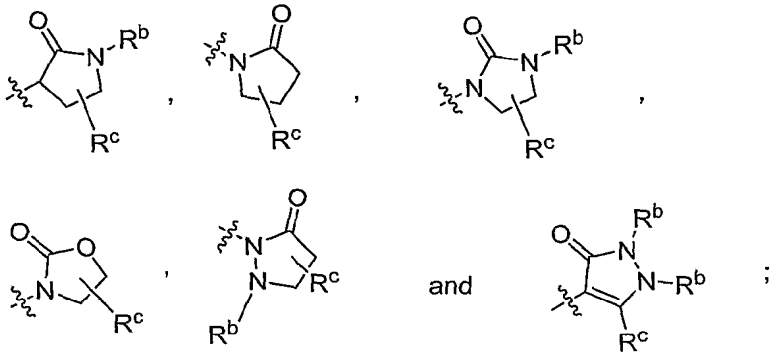
R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein

R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; or wherein

two R^c substituents, two R^b substituents or R^c together with R^b together form an optionally substituted fused phenyl ring; or wherein two R^c substituents, together form an optionally substituted 3-6 membered spiro ring; in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

R^1 is selected from



R^b is independently selected at each occurrence from H, optionally substituted arylalkyl, optionally substituted 5-6-membered heterocyclyl-C_{1-3} alkyl, optionally substituted C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted C_{6-10} ary, optionally substituted C_{6-10} heteroaryl, optionally substituted C_{3-6} cycloalkyl, and $R^aR^{5a}N$-C_{1-3}alkyl;

R^c is one or more substituents selected from H, methyl, isopropyl, tert-butyl, bromo, fluoro, hydroxyl, $R^{5a}R^aN$-, $R^{5a}R^aN$-C_{1-3} alkyl, methoxymethyl, methoxyethyl, methylthiomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, optionally substituted phenyl, optionally substituted pyridyl, optionally substituted thienyl, and optionally substituted benzyl; wherein R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; C_{6-10} aryl, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, $-C(=O)R^{5a}$ and optionally substituted heteroraryl

R^a is selected from H, C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, optionally substituted phenyl-C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl-C_{1-6}-alkyl, C_{3-6}-cycloalkyl, C_{3-6}-cycloalkyl-C_{1-6}-alkyl, C_{2-6}-alkenyl and C_{2-6}-alkynyl; and

R^{5a} is selected from H, C_{1-6}-alkyl, C_{1-6}-haloalkyl, phenyl-C_{1-6}-alkyl, 5-6 membered heterocyclyl-C_{1-6}-alkyl, C_{3-6}-cycloalkyl-C_{1-6}-alkyl, $R^aC(=O)$-, optionally substituted phenyl, optionally substituted 5-6-membered heterocyclyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl and C_{3-6}-cycloalkyl; or wherein

two adjacent R^c substituents, two adjacent R^b substituents or R^c together with an adjacent R^b together form an optionally substituted fused ring; or wherein two R^c substituents, together

form an optionally substituted spiro ring; in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

R^b is selected from H, optionally substituted benzyl, C_{1-3} alkylaryl, C_{1-3} alkylheteroaryl, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, methoxymethyl,, -(C_{1-6})alkyl,2-hydroxy 2-methylbutyl, 2-hydroxy-2-methylpropyl, 2-hydroxypropyl, 1-(1-hydroxycyclopropyl)methyl,, ethylaminomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, pyridyl, thienyl, optionally substituted phenyl,1-naphthy, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, and $-C(=O)R^{5a}$;

R^c is one or more substituents selected from H, methyl, isopropyl, tert-butyl, bromo, fluoro, hydroxyl, $R^{5a}R^aN$-, $R^{5a}R^aN$-C_{1-3} alkyl, methoxymethyl, methoxyethyl, methylthiomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, optionally substituted phenyl, optionally substituted pyridyl, optionally substituted thienyl, and optionally substituted benzyl; wherein R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; C_{6-10} aryl, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, $-C(=O)R^{5a}$ and optionally substituted heteroraryl

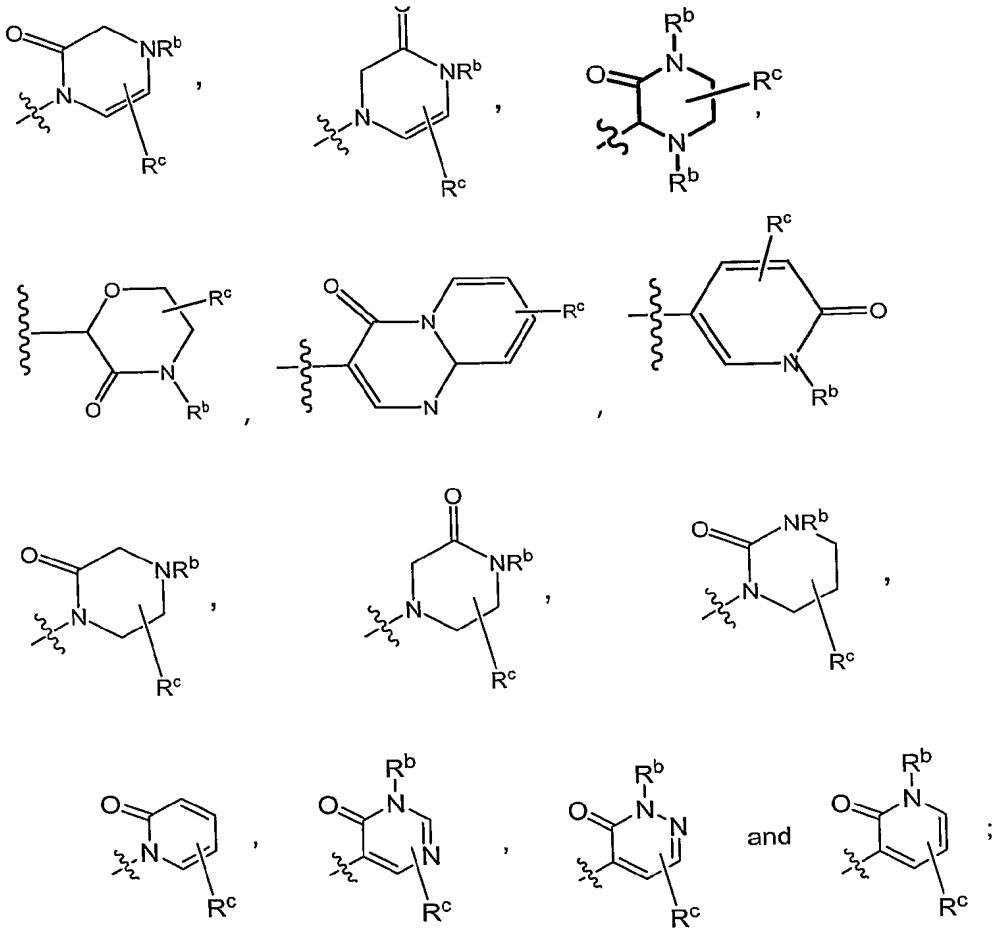
R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein

R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; or wherein two R^c substituents, two R^b substituents or R^c together with R^b together form an optionally substituted fused phenyl ring; or wherein

two R^c substituents, together form an optionally substituted 3-6 membered spiro ring; in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

R^1 is selected from



R^b is independently selected at each occurrence from H, optionally substituted arylalkyl, optionally substituted 5-6-membered heterocyclyl-C_{1-3} alkyl, optionally substituted C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted C_{6-10} ary, optionally substituted C_{6-10} heteroaryl, optionally substituted C_{3-6} cycloalkyl, and $R^aR^{5a}N$-C_{1-3}alkyl;

R^c is one or more substituents selected from H, methyl, isopropyl, tert-butyl, bromo, fluoro, hydroxyl, $R^{5a}R^aN$-, $R^{5a}R^aN$-C_{1-3} alkyl, methoxymethyl, methoxyethyl, methylthiomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, optionally substituted phenyl, optionally substituted pyridyl, optionally substituted thienyl, and optionally substituted benzyl; wherein R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; C_{6-10} aryl, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, $-C(=O)R^{5a}$ and optionally substituted heteroraryl

R^a is selected from H, C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, optionally substituted phenyl-C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl-C_{1-6}-alkyl, C_{3-6}-cycloalkyl, C_{3-6}-cycloalkyl-C_{1-6}-alkyl, C_{2-6}-alkenyl and C_{2-6}-alkynyl; and

R^{5a} is selected from H, C_{1-6}-alkyl, C_{1-6}-haloalkyl, phenyl-C_{1-6}-alkyl, 5-6 membered heterocyclyl-C_{1-6}-alkyl, C_{3-6}-cycloalkyl-C_{1-6}-alkyl, $R^aC(=O)$-, optionally substituted phenyl, optionally substituted 5-6-membered heterocyclyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl and C_{3-6}-cycloalkyl; or wherein

two adjacent R^c substituents, two adjacent R^b substituents or R^c together with an adjacent R^b together form an optionally substituted fused ring; or wherein

two R^c substituents, together form an optionally substituted spiro ring; in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

R^b is selected from H, optionally substituted benzyl, C_{1-3} alkylaryl, C_{1-3} alkylheteroaryl, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, methoxymethyl,, -(C_{1-6})alkyl,2-hydroxy 2-methylbutyl, 2-hydroxy-2-methylpropyl, 2-hydroxypropyl, 1-(1-hydroxycyclopropyl)methyl,, ethylaminomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, pyridyl, thienyl, optionally substituted phenyl,1-naphthy, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, and $-C(=O)R^{5a}$;

R^c is one or more substituents selected from H, methyl, isopropyl, tert-butyl, bromo, fluoro, hydroxyl, $R^{5a}R^aN$-, $R^{5a}R^aN$-C_{1-3} alkyl, methoxymethyl, methoxyethyl, methylthiomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, optionally substituted phenyl, optionally substituted pyridyl, optionally substituted thienyl, and optionally substituted benzyl; wherein R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; C_{6-10} aryl, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, $-C(=O)R^{5a}$ and optionally substituted heteroraryl

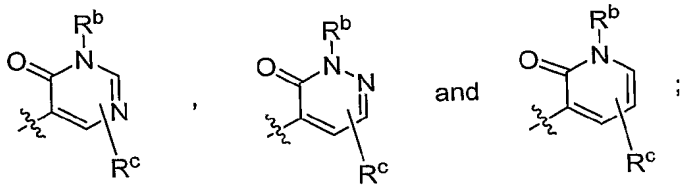
R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; or wherein

two R^c substituents, two R^b substituents or R^c together with R^b together form an optionally substituted fused phenyl ring; or wherein

two R^c substituents, together form an optionally substituted 3-6 membered spiro ring; in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

R^1 is selected from



wherein

R^b is independently selected at each occurrence from H, optionally substituted arylalkyl, optionally substituted 5-6-membered heterocyclyl-C_{1-3} alkyl, optionally substituted C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted C_{6-10} ary, optionally substituted C_{6-10} heteroaryl, optionally substituted C_{3-6} cycloalkyl, and $R^aR^{5a}N$-C_{1-3}alkyl;

R^c is one or more substituents selected from H, methyl, isopropyl, tert-butyl, bromo, fluoro, hydroxyl, $R^{5a}R^aN$-, $R^{5a}R^aN$-C_{1-3} alkyl, methoxymethyl, methoxyethyl, methylthiomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, optionally substituted phenyl, optionally substituted pyridyl, optionally substituted thienyl, and optionally substituted benzyl; wherein R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; C_{6-10} aryl, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, $-C(=O)R^{5a}$ and optionally substituted heteroraryl

R^a is selected from H, C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, optionally substituted phenyl-C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl-C_{1-6}-alkyl, C_{3-6}-cycloalkyl, C_{3-6}-cycloalkyl-C_{1-6}-alkyl, C_{2-6}-alkenyl and C_{2-6}-alkynyl; and

R^{5a} is selected from H, C_{1-6}-alkyl, C_{1-6}-haloalkyl, phenyl-C_{1-6}-alkyl, 5-6 membered heterocyclyl-C_{1-6}-alkyl, C_{3-6}-cycloalkyl-C_{1-6}-alkyl, $R^aC(=O)$-, optionally substituted phenyl, optionally substituted 5-6-membered heterocyclyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl and C_{3-6}-cycloalkyl; or wherein

two adjacent R^c substituents, two adjacent R^b substituents or R^c together with an adjacent R^b together form an optionally substituted fused ring; or wherein two R^c substituents, together

form an optionally substituted spiro ring; in conjunction with any of the above or below embodiments.

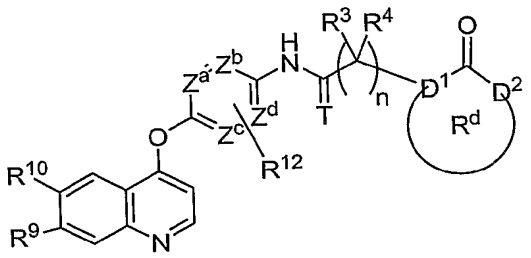
The invention also relates to compounds wherein

R^b is selected from H, optionally substituted benzyl, C_{1-3} alkylaryl, C_{1-3} alkylheteroaryl, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, methoxymethyl,, -(C_{1-6})alkyl,2-hydroxy 2-methylbutyl, 2-hydroxy-2-methylpropyl, 2-hydroxypropyl, 1-(1-hydroxycyclopropyl)methyl,, ethylaminomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, pyridyl, thienyl, optionally substituted phenyl,1-naphthy, nitrile, -C(=O)OR^{5a}, -C(=O)$NR^{5a}R^a$, and -C(=O)R^{5a} ;

R^c is one or more substituents selected from H, methyl, isopropyl, tert-butyl, bromo, fluoro, hydroxyl, $R^{5a}R^aN$-, $R^{5a}R^aN$-C_{1-3} alkyl, methoxymethyl, methoxyethyl, methylthiomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, optionally substituted phenyl, optionally substituted pyridyl, optionally substituted thienyl, and optionally substituted benzyl; wherein R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; C_{6-10} aryl, nitrile, -C(=O)OR^{5a}, -C(=O)$NR^{5a}R^a$, -C(=O)R^{5a} and optionally substituted heteroraryl

R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; or wherein two R^c substituents, two R^b substituents or R^c together with R^b together form an optionally substituted fused phenyl ring; or wherein two R^c substituents, together form an optionally substituted 3-6 membered spiro ring; in conjunction with any of the above or below embodiments.

The invention also relates to compounds of Formula II



II

wherein

T is O or S;

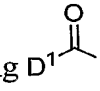
R^3 and R^4 is each independently selected from H, C_{1-2}-alkyl, phenyl, 5-6-membered heterocyclyl, phenyl-C_{1-2}-alkyl, 5-6-membered heterocyclyl- C_{1-2}-alkyl, C_{3-6}-cycloalkyl, and C_{3-6}-cycloalkyl-C_{1-2}-alkyl; alternatively R^3 and R^4, together with the atom they are attached to, form an optionally substituted 4-6 membered ring;

R^9 and R^{10} is independently selected from H, cyano, hydroxy, $-C(=O)NR^aR^{5a}$, 5-6 membered heterocyclyl, $-NR^aC(=O)-R^{5a}$, $R^{5a}R^aN-O_2S-$, $R^{5a}O_2SR^aN-$, $R^{5a}R^aN-$, C_{1-6}-alkyl, amino-C_{1-6}-alkyl, C_{1-6}-alkylamino-C_{1-6}-alkyl, alkoxy-C_{1-6}-alkyl, hydroxy, aryl-C_{1-6}-alkyl, heterocyclyl-C_{1-6}-alkyl, C_{1-6}-alkoxy, halo-C_{1-6}-alkoxy, C_{1-6}-alkylamino-C_{1-6}-alkoxy, aryl-C_{1-6}-alkoxy, 5-6-membered heterocyclyl, -C_{1-6}alkoxy, C_{3-6}-cycloalkyl-C_{1-6}-alkoxy, 5-6-membered heterocyclyl(hydroxyl-C_{1-6}-alkoxy), C_{3-6}-cycloalkyl(hydroxyl-C_{1-6}-alkoxy), phenyl(hydroxyl-C_{1-6}-alkoxy), C_{1-6}-alkoxy-C_{1-6}-alkoxy, phenyloxy-C_{1-6}-alkoxy, 5-6 membered heterocyclyloxy-C_{1-6}-alkoxy, C_{3-6}-cycloalkyloxy-C_{1-6}-alkoxy, phenyloxy, 5-6-membered heterocyclyloxy, and C_{3-6}-cycloalkyloxy; each of Z^a, Z^b, Z^c and Z^d is independently selected from N or CH; provided no more than 2 of Z^a, Z^b, Z^c and Z^d are N;

n is 0, 1, 2 or 3;

D^1 is selected from N or CR^{11};

D^2 is selected from NR^{13}, O, or CHR^{11}; provided either D^1 is N or D^2 is NR^{13};

ring R^d including  forms an optionally substituted optionally benzo-fused 4-7 membered heterocyclic moiety,

R^{11} is selected from H, halo, C_{1-4}-alkyl, C_{1-4}-haloalkyl, C_{1-4}-hydroxyalkyl, $-NH_2$, $-OR^{12}$, alkoxycarbonyl, $-CO_2H$, $-CONR^3R^{5a}$, (C_1-C_3)alkylamino, di(C_1-C_6)alkylamino, (C_1-C_3)hydroxyalkylamino, (C_1-C_3)alkylamino-(C_1-C_3)alkylamino, C_{1-3}-alkoxy-C_{1-3}-alkyl, C_{1-3}-alkylamino-C_{1-3}-alkyl, C_{1-3}-alkylthio-C_{1-3}-alkyl, optionally substituted phenyl-C_{1-3}-alkyl, 5-6 membered heterocyclyl-C_{1-3}-alkyl, C_{3-6}-cycloalkyl-C_{1-3}-alkyl, optionally substituted phenyl, optionally substituted 5-6 membered heterocyclyl, and C_{3-6}-cycloalkyl;

R^a is selected from H, alkyl, heterocyclyl, aryl, arylalkyl, heterocyclylalkyl, cycloalkyl, cycloalkylalkyl, alkenyl and alkynyl;

R^{5a} is selected from H, alkyl, haloalkyl, arylalkyl, heterocyclylalkyl, cycloalkylalkyl, aryl, heterocyclyl, alkenyl, alkynyl and cycloalkyl;

R^{12} is selected from H, halo, C_{1-2}-alkyl and methoxy;

R^{13} is selected from H, alkyl, haloalkyl, optionally substituted phenylalkyl, optionally substituted 5-10 membered heterocyclylalkyl, cycloalkylalkyl, optionally substituted phenyl or naphthyl, optionally substituted 5-10 membered heterocyclyl and cycloalkyl.

The invention also relates to compounds wherein

R^9 and R^{10} are independently selected from H, cyano, aminocarbonyl, C_{1-3}-alkylaminocarbonyl, C_{1-3}-alkylamino-C_{1-3}-alkoxy, 5-6 membered heterocyclyl-C_{1-3}-alkoxy, C_{4-6}-cycloalkyl-C_{1-3}-alkoxy, 5-6 membered heterocyclyl-C_{1-3}-(hydroxyalkoxy), C_{3-6}-cycloalkyl-C_{1-3}-(hydroxyalkoxy), C_{1-2}-alkoxy-C_{1-3}-alkoxy, phenyloxy-C_{1-3}alkoxy, 5-6 membered heterocyclyloxy-C_{1-3}-alkoxy, cycloalkyloxy-C_{1-3}-alkoxy, 5-6 membered heterocyclyloxy, and C_{3-6}-cycloalkyloxy; in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

R^9 is independently selected from H, methyl, cyano, aminocarbonyl, methylaminocarbonyl, methoxy, dimethylaminopropoxy, 3-(morpholin-4-yl)ethoxy, 3-(pyrrolidin-1-yl)propoxy, 2-hydroxy-3-(morpholin-4-yl)propoxy, 3-(1,2,4-triazol-1-yl)propoxy, 3-(4-methylpiperazin-1-yl)propoxy, 3-(piperidin-4-yl)propoxy, dimethylaminoethoxy and diethylaminoethoxy; in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

R^{10} is methoxy; in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

Z^a is CH; wherein Z^b is CH; wherein Z^c is CF; and wherein Z^d is CH; in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

Z^a is N;

Z^a is CH;

Z^c is CH;

Z^d is CH; and

R^{12} is H; in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

Z^a is CH;

Z^b is N;

Z^c is CH;

Z^d is CH; and

R^{12} is H; in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

Z^a is CH;

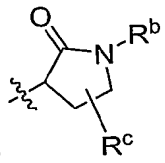
Z^b is N;

Z^c is CH;

Z^d is N; and

R^{12} is H; in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

R^d is  ;

R^b is independently selected at each occurrence from H, optionally substituted arylalkyl, optionally substituted 5-6-membered heterocyclyl-C_{1-3} alkyl, optionally substituted C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted C_{6-10} ary, optionally substituted C_{6-10} heteroaryl, optionally substituted C_{3-6} cycloalkyl, and $R^aR^{5a}N$-C_{1-3}alkyl;

R^c is one or more substituents selected from H, methyl, isopropyl, tert-butyl, bromo, fluoro, hydroxyl, $R^{5a}R^aN$-, $R^{5a}R^aN$-C_{1-3} alkyl, methoxymethyl, methoxyethyl, methylthiomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, optionally substituted phenyl, optionally substituted pyridyl, optionally substituted thienyl, and optionally substituted benzyl; wherein R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; C_{6-10} aryl, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, $-C(=O)R^{5a}$ and optionally substituted heteroraryl

R^a is selected from H, C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, optionally substituted phenyl-C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl-C_{1-6}-alkyl, C_{3-6}-cycloalkyl, C_{3-6}-cycloalkyl-C_{1-6}-alkyl, C_{2-6}-alkenyl and C_{2-6}-alkynyl; and

R^{5a} is selected from H, C_{1-6}-alkyl, C_{1-6}-haloalkyl, phenyl-C_{1-6}-alkyl, 5-6 membered heterocyclyl-C_{1-6}-alkyl, C_{3-6}-cycloalkyl-C_{1-6}-alkyl, optionally substituted phenyl, optionally substituted 5-6-membered heterocyclyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl and C_{3-6}-cycloalkyl; or wherein

two adjacent R^c substituents, two adjacent R^b substituents or R^c together with an adjacent R^b together form an optionally substituted fused phenyl ring; or wherein

two R^c substituents, together form an optionally substituted spiro ring;

in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

R^b is selected from H, optionally substituted benzyl, C_{1-3} alkylaryl, C_{1-3} alkylheteroaryl, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, methoxymethyl,, -(C_{1-6})alkyl,2-hydroxy 2-methylbutyl, 2-hydroxy-2-methylpropyl, 2-hydroxypropyl, 1-(1-hydroxycyclopropyl)methyl,, ethylaminomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, pyridyl, thienyl, optionally substituted phenyl,1-naphthy, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, and $-C(=O)R^{5a}$;

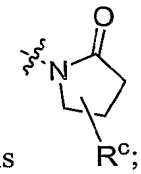
R^c is one or more substituents selected from H, methyl, isopropyl, tert-butyl, bromo, fluoro, hydroxyl, $R^{5a}R^aN$-, $R^{5a}R^aN$-C_{1-3} alkyl, methoxymethyl, methoxyethyl, methylthiomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, optionally substituted phenyl, optionally substituted pyridyl, optionally substituted thienyl, and optionally substituted benzyl; wherein R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; C_{6-10} aryl, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, $-C(=O)R^{5a}$ and optionally substituted heteroraryl

R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; or

two R^c substituents, two R^b substituents or R^c together with R^b together form an optionally substituted fused phenyl ring; or

two R^c substituents, together form an optionally substituted 3-6 membered spiro ring; in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

R^d is  ; wherein

R^c is one or more substituents selected from H, methyl, isopropyl, tert-butyl, bromo, fluoro, hydroxyl, $R^{5a}R^aN$-, $R^{5a}R^aN$-C_{1-3} alkyl, methoxymethyl, methoxyethyl, methylthiomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, optionally substituted phenyl, optionally substituted pyridyl, optionally substituted thienyl, and optionally substituted benzyl; wherein R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; C_{6-10} aryl, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, $-C(=O)R^{5a}$ and optionally substituted heteroraryl

R^a is selected from H, C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, optionally substituted phenyl-C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl-C_{1-6}-alkyl, C_{3-6}-cycloalkyl, C_{3-6}-cycloalkyl-C_{1-6}-alkyl, C_{2-6}-alkenyl and C_{2-6}-alkynyl; and

R^{5a} is selected from H, C_{1-6}-alkyl, C_{1-6}-haloalkyl, phenyl-C_{1-6}-alkyl, 5-6 membered heterocyclyl-C_{1-6}-alkyl, C_{3-6}-cycloalkyl-C_{1-6}-alkyl, $R^aC(=O)$-, optionally substituted phenyl, optionally substituted 5-6-membered heterocyclyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl and C_{3-6}-cycloalkyl;or wherein

two adjacent R^c substituents, two adjacent R^b substituents or R^c together with an adjacent R^b together form an optionally substituted fused phenyl ring; or wherein

two R^c substituents, together form an optionally substituted spiro ring;

in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

R^c is one or more substituents selected from H, methyl, isopropyl, tert-butyl, bromo, fluoro, hydroxyl, $R^{5a}R^aN$-, $R^{5a}R^aN$-C_{1-3} alkyl, methoxymethyl, methoxyethyl, methylthiomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, optionally substituted phenyl, optionally substituted pyridyl, optionally substituted thienyl, and optionally substituted benzyl; wherein R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; C_{6-10} aryl, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, $-C(=O)R^{5a}$ and optionally substituted heteroraryl

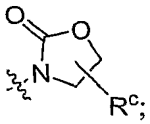
R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; C_{6-10} aryl, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, $-C(=O)R^{5a}$ and optionally substituted heteroraryl

R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; or

two R^c substituents, two R^b substituents or R^c together with R^b together form an optionally substituted fused phenyl ring; or wherein two R^c substituents, together form an optionally substituted 3-6 membered spiro ring;

in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

R^d is  ;

R^c is one or more substituents selected from H, methyl, isopropyl, tert-butyl, bromo, fluoro, hydroxyl, $R^{5a}R^aN$-, $R^{5a}R^aN$-C_{1-3} alkyl, methoxymethyl, methoxyethyl, methylthiomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, optionally substituted phenyl, optionally substituted pyridyl, optionally substituted thienyl, and optionally substituted benzyl; wherein R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; C_{6-10} aryl, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, $-C(=O)R^{5a}$ and optionally substituted heteroraryl

R^a is selected from H, C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, optionally substituted phenyl-C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl-C_{1-6}-alkyl, C_{3-6}-cycloalkyl, C_{3-6}-cycloalkyl-C_{1-6}-alkyl, C_{2-6}-alkenyl and C_{2-6}-alkynyl; and

R^{5a} is selected from H, C_{1-6}-alkyl, C_{1-6}-haloalkyl, phenyl-C_{1-6}-alkyl, 5-6 membered heterocyclyl-C_{1-6}-alkyl, C_{3-6}-cycloalkyl-C_{1-6}-alkyl, $R^aC(=O)$-, optionally substituted

phenyl, optionally substituted 5-6-membered heterocyclyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl and C_{3-6}-cycloalkyl; or wherein

two adjacent R^c substituents, two adjacent R^b substituents or R^c together with an adjacent R^b together form an optionally substituted fused phenyl ring; or wherein

two R^c substituents, together form an optionally substituted spiro ring;

in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

R^c is one or more substituents selected from H, methyl, isopropyl, tert-butyl, bromo, fluoro, hydroxyl, $R^{5a}R^aN$-, $R^{5a}R^aN$-C_{1-3} alkyl, methoxymethyl, methoxyethyl, methylthiomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, optionally substituted phenyl, optionally substituted pyridyl, optionally substituted thienyl, and optionally substituted benzyl; wherein R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; C_{6-10} aryl, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, $-C(=O)R^{5a}$ and optionally substituted heteroraryl

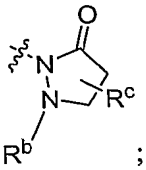
R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; or

two R^c substituents, two R^b substituents or R^c together with R^b together form an optionally substituted fused phenyl ring; or

two R^c substituents, together form an optionally substituted 3-6 membered spiro ring;

in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein



R^d is R^b ;

R^b is independently selected at each occurrence from H, optionally substituted arylalkyl, optionally substituted 5-6-membered heterocyclyl-C_{1-3} alkyl, optionally substituted C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted C_{6-10} ary,

optionally substituted C_{6-10} heteroaryl, optionally substituted C_{3-6} cycloalkyl, and $R^aR^{5a}N$-C_{1-3}alkyl;

R^c is one or more substituents selected from H, methyl, isopropyl, tert-butyl, bromo, fluoro, hydroxyl, $R^{5a}R^aN$-, $R^{5a}R^aN$-C_{1-3} alkyl, methoxymethyl, methoxyethyl, methylthiomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, optionally substituted phenyl, optionally substituted pyridyl, optionally substituted thienyl, and optionally substituted benzyl; wherein R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; C_{6-10} aryl, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, $-C(=O)R^{5a}$ and optionally substituted heteroraryl

R^a is selected from H, C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, optionally substituted phenyl-C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl-C_{1-6}-alkyl, C_{3-6}-cycloalkyl, C_{3-6}-cycloalkyl-C_{1-6}-alkyl, C_{2-6}-alkenyl and C_{2-6}-alkynyl; and

R^{5a} is selected from H, C_{1-6}-alkyl, C_{1-6}-haloalkyl, phenyl-C_{1-6}-alkyl, 5-6 membered heterocyclyl-C_{1-6}-alkyl, C_{3-6}-cycloalkyl-C_{1-6}-alkyl, $R^aC(=O)$-, optionally substituted phenyl, optionally substituted 5-6-membered heterocyclyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl and C_{3-6}-cycloalkyl; or wherein

two adjacent R^c substituents, two adjacent R^b substituents or R^c together with an adjacent R^b together form an optionally substituted fused phenyl ring; or wherein

two R^c substituents, together form an optionally substituted spiro ring;

in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

R^b is selected from H, optionally substituted benzyl, C_{1-3} alkylaryl, C_{1-3} alkylheteroaryl, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, methoxymethyl,, -(C_{1-6})alkyl,2-hydroxy 2-methylbutyl, 2-hydroxy-2-methylpropyl, 2-hydroxypropyl, 1-(1-hydroxycyclopropyl)methyl,, ethylaminomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, pyridyl, thienyl, optionally substituted phenyl,1-naphthy, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, and $-C(=O)R^{5a}$;

R^c is one or more substituents selected from H, methyl, isopropyl, tert-butyl, bromo, fluoro, hydroxyl, $R^{5a}R^aN$-, $R^{5a}R^aN$-C_{1-3} alkyl, methoxymethyl, methoxyethyl, methylthiomethyl,

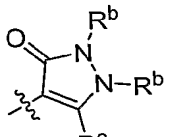
piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, optionally substituted phenyl, optionally substituted pyridyl, optionally substituted thienyl, optionally substituted benzyl, and ;

R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and

R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; or wherein two R^c substituents, two R^b substituents or R^c together with R^b together form an optionally substituted fused phenyl ring; or wherein

two R^c substituents, together form an optionally substituted 3-6 membered spiro ring; in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

R^d is  ;

R^b is independently selected at each occurrence from H, optionally substituted arylalkyl, optionally substituted 5-6-membered heterocyclyl-C_{1-3} alkyl, optionally substituted C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted C_{6-10} ary, optionally substituted C_{6-10} heteroaryl, optionally substituted C_{3-6} cycloalkyl, and $R^aR^{5a}N$-C_{1-3}alkyl;

R^c is one or more substituents selected from H, methyl, isopropyl, tert-butyl, bromo, fluoro, hydroxyl, $R^{5a}R^aN$-, $R^{5a}R^aN$-C_{1-3} alkyl, methoxymethyl, methoxyethyl, methylthiomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, optionally substituted phenyl, optionally substituted pyridyl, optionally substituted thienyl, and optionally substituted benzyl; wherein R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; C_{6-10} aryl, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, $-C(=O)R^{5a}$ and optionally substituted heteroraryl

R^a is selected from H, C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, optionally substituted phenyl-C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl-C_{1-6}-alkyl, C_{3-6}-cycloalkyl, C_{3-6}-cycloalkyl-C_{1-6}-alkyl, C_{2-6}-alkenyl and C_{2-6}-alkynyl; and

R^{5a} is selected from H, C_{1-6}-alkyl, C_{1-6}-haloalkyl, phenyl-C_{1-6}-alkyl, 5-6 membered heterocyclyl-C_{1-6}-alkyl, C_{3-6}-cycloalkyl-C_{1-6}-alkyl, $R^aC(=O)$-, optionally substituted phenyl, optionally substituted 5-6-membered heterocyclyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl and C_{3-6}-cycloalkyl;or wherein

two adjacent R^c substituents, two adjacent R^b substituents or R^c together with an adjacent R^b together form an optionally substituted fused phenyl ring; or wherein

two R^c substituents, together form an optionally substituted spiro ring;

in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

R^b is selected from H, optionally substituted benzyl, C_{1-3} alkylaryl, C_{1-3} alkylheteroaryl, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, methoxymethyl,, -(C_{1-6})alkyl,2-hydroxy 2-methylbutyl, 2-hydroxy-2-methylpropyl, 2-hydroxypropyl, 1-(1-hydroxycyclopropyl)methyl,, ethylaminomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, pyridyl, thienyl, optionally substituted phenyl,1-naphthy, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, and $-C(=O)R^{5a}$;

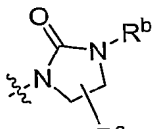
R^c is one or more substituents selected from H, methyl, isopropyl, tert-butyl, bromo, fluoro, hydroxyl, $R^{5a}R^aN$-, $R^{5a}R^aN$-C_{1-3} alkyl, methoxymethyl, methoxyethyl, methylthiomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, optionally substituted phenyl, optionally substituted pyridyl, optionally substituted thienyl, and optionally substituted benzyl; wherein R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; C_{6-10} aryl, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, $-C(=O)R^{5a}$ and optionally substituted heteroraryl

R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; or wherein

two R^c substituents, two R^b substituents or R^c together with R^b together form an optionally substituted fused phenyl ring; or wherein

two R^c substituents, together form an optionally substituted 3-6 membered spiro ring; in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein



R^d is ;

R^b is independently selected at each occurrence from H, optionally substituted arylalkyl, optionally substituted 5-6-membered heterocyclyl-C_{1-3} alkyl, optionally substituted C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted C_{6-10} ary, optionally substituted C_{6-10} heteroaryl, optionally substituted C_{3-6} cycloalkyl, and $R^aR^{5a}N$-C_{1-3}alkyl;

R^c is one or more substituents selected from H, methyl, isopropyl, tert-butyl, bromo, fluoro, hydroxyl, $R^{5a}R^aN$-, $R^{5a}R^aN$-C_{1-3} alkyl, methoxymethyl, methoxyethyl, methylthiomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, optionally substituted phenyl, optionally substituted pyridyl, optionally substituted thienyl, and optionally substituted benzyl; wherein R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; C_{6-10} aryl, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, $-C(=O)R^{5a}$ and optionally substituted heteroraryl

R^a is selected from H, C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, optionally substituted phenyl-C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl-C_{1-6}-alkyl, C_{3-6}-cycloalkyl, C_{3-6}-cycloalkyl-C_{1-6}-alkyl, C_{2-6}-alkenyl and C_{2-6}-alkynyl; and

R^{5a} is selected from H, C_{1-6}-alkyl, C_{1-6}-haloalkyl, phenyl-C_{1-6}-alkyl, 5-6 membered heterocyclyl-C_{1-6}-alkyl, C_{3-6}-cycloalkyl-C_{1-6}-alkyl, $R^aC(=O)$-, optionally substituted phenyl, optionally substituted 5-6-membered heterocyclyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl and C_{3-6}-cycloalkyl; or wherein

two adjacent R^c substituents, two adjacent R^b substituents or R^c together with an adjacent R^b together form an optionally substituted fused phenyl ring; or wherein

two R^c substituents, together form an optionally substituted spiro ring;

in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

R^b is selected from H, optionally substituted benzyl, C_{1-3} alkylaryl, C_{1-3} alkylheteroaryl, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, methoxymethyl,, -(C_{1-6})alkyl,2-hydroxy 2-

methylbutyl, 2-hydroxy-2-methylpropyl, 2-hydroxypropyl, 1-(1-hydroxycyclopropyl)methyl,, ethylaminomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, pyridyl, thienyl, optionally substituted phenyl,1-naphthy, nitrile, -C(=O)OR^{5a}, -C(=O)$NR^{5a}R^a$, and -C(=O)R^{5a} ;

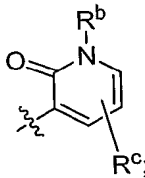
R^c is one or more substituents selected from H, methyl, isopropyl, tert-butyl, bromo, fluoro, hydroxyl, $R^{5a}R^aN$-, $R^{5a}R^aN$-C_{1-3} alkyl, methoxymethyl, methoxyethyl, methylthiomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, optionally substituted phenyl, optionally substituted pyridyl, optionally substituted thienyl, and optionally substituted benzyl; wherein R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; or wherein

two R^c substituents, two R^b substituents or R^c together with R^b together form an optionally substituted fused phenyl ring; or wherein

two R^c substituents, together form an optionally substituted 3-6 membered spiro ring;

in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein



R^d is R^c;

R^b is independently selected at each occurrence from H, optionally substituted arylalkyl, optionally substituted 5-6-membered heterocyclyl-C_{1-3} alkyl, optionally substituted C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted C_{6-10} ary, optionally substituted C_{6-10} heteroaryl, optionally substituted C_{3-6} cycloalkyl, and $R^aR^{5a}N$-C_{1-3}alkyl;

R^c is one or more substituents selected from H, methyl, isopropyl, tert-butyl, bromo, fluoro, hydroxyl, $R^{5a}R^aN$-, $R^{5a}R^aN$-C_{1-3} alkyl, methoxymethyl, methoxyethyl, methylthiomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, optionally substituted phenyl, optionally substituted pyridyl, optionally substituted thienyl, and optionally substituted benzyl; wherein R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-

alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; C_{6-10} aryl, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, $-C(=O)R^{5a}$ and optionally substituted heteroraryl

R^a is selected from H, C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, optionally substituted phenyl-C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl-C_{1-6}-alkyl, C_{3-6}-cycloalkyl, C_{3-6}-cycloalkyl-C_{1-6}-alkyl, C_{2-6}-alkenyl and C_{2-6}-alkynyl; and

R^{5a} is selected from H, C_{1-6}-alkyl, C_{1-6}-haloalkyl, phenyl-C_{1-6}-alkyl, 5-6 membered heterocyclyl-C_{1-6}-alkyl, C_{3-6}-cycloalkyl-C_{1-6}-alkyl, $R^aC(=O)$-, optionally substituted phenyl, optionally substituted 5-6-membered heterocyclyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl and C_{3-6}-cycloalkyl;or wherein

two adjacent R^c substituents, two adjacent R^b substituents or R^c together with an adjacent R^b together form an optionally substituted fused phenyl ring; or wherein

two R^c substituents, together form an optionally substituted spiro ring;

in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

R^b is selected from H, optionally substituted benzyl, C_{1-3} alkylaryl, C_{1-3} alkylheteroaryl, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, methoxymethyl,, -(C_{1-6})alkyl,2-hydroxy 2-methylbutyl, 2-hydroxy-2-methylpropyl, 2-hydroxypropyl, 1-(1-hydroxycyclopropyl)methyl,, ethylaminomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, pyridyl, thienyl, optionally substituted phenyl,1-naphthy, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, and $-C(=O)R^{5a}$;

R^c is one or more substituents selected from H, methyl, isopropyl, tert-butyl, bromo, fluoro, hydroxyl, $R^{5a}R^aN$-, $R^{5a}R^aN$-C_{1-3} alkyl, methoxymethyl, methoxyethyl, methylthiomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, optionally substituted phenyl, optionally substituted pyridyl, optionally substituted thienyl, and optionally substituted benzyl;

wherein R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; C_{6-10} aryl, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, $-C(=O)R^{5a}$ and optionally substituted heteroraryl

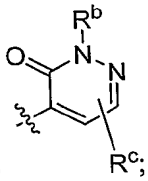
R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-

butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; or wherein

two R^c substituents, two R^b substituents or R^c together with R^b together form an optionally substituted fused phenyl ring; or wherein

two R^c substituents, together form an optionally substituted 3-6 membered spiro ring; in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein



R^d is

R^b is independently selected at each occurrence from H, optionally substituted arylalkyl, optionally substituted 5-6-membered heterocyclyl-C_{1-3} alkyl, optionally substituted C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted C_{6-10} ary, optionally substituted C_{6-10} heteroaryl, optionally substituted C_{3-6} cycloalkyl, and $R^aR^{5a}N$-C_{1-3}alkyl;

R^c is one or more substituents selected from H, methyl, isopropyl, tert-butyl, bromo, fluoro, hydroxyl, $R^{5a}R^aN$-, $R^{5a}R^aN$-C_{1-3} alkyl, methoxymethyl, methoxyethyl, methylthiomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, optionally substituted phenyl, optionally substituted pyridyl, optionally substituted thienyl, and optionally substituted benzyl; wherein R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; C_{6-10} aryl, nitrile, $-C(=O)OR^{5a}$, $-C(=O)NR^{5a}R^a$, $-C(=O)R^{5a}$ and optionally substituted heteroraryl

R^a is selected from H, C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, optionally substituted phenyl-C_{1-6}-alkyl, optionally substituted 5-6 membered heterocyclyl-C_{1-6}-alkyl, C_{3-6}-cycloalkyl, C_{3-6}-cycloalkyl-C_{1-6}-alkyl, C_{2-6}-alkenyl and C_{2-6}-alkynyl; and

R^{5a} is selected from H, C_{1-6}-alkyl, C_{1-6}-haloalkyl, phenyl-C_{1-6}-alkyl, 5-6 membered heterocyclyl-C_{1-6}-alkyl, C_{3-6}-cycloalkyl-C_{1-6}-alkyl, $R^aC(=O)$-, optionally substituted

phenyl, optionally substituted 5-6-membered heterocyclyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl and C_{3-6}-cycloalkyl;or wherein

two adjacent R^c substituents, two adjacent R^b substituents or R^c together with an adjacent R^b together form an optionally substituted fused phenyl ring; or wherein

two R^c substituents, together form an optionally substituted spiro ring;

in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

R^b is selected from H, optionally substituted benzyl, C_{1-3} alkylaryl, C_{1-3} alkylheteroaryl, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, methoxymethyl,, -(C_{1-6})alkyl,2-hydroxy 2-methylbutyl, 2-hydroxy-2-methylpropyl, 2-hydroxypropyl, 1-(1-hydroxycyclopropyl)methyl,, ethylaminomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, pyridyl, thienyl, optionally substituted phenyl,1-naphthy, nitrile, -C(=O)OR^{5a}, -C(=O)$NR^{5a}R^a$, and -C(=O)R^{5a} ;

R^c is one or more substituents selected from H, methyl, isopropyl, tert-butyl, bromo, fluoro, hydroxyl, $R^{5a}R^aN$-, $R^{5a}R^aN$-C_{1-3} alkyl, methoxymethyl, methoxyethyl, methylthiomethyl, piperidin-1-ylmethyl, pyrrolidin-1-ylmethyl, optionally substituted phenyl, optionally substituted pyridyl, optionally substituted thienyl, and optionally substituted benzyl; wherein R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; C_{6-10} aryl, nitrile, -C(=O)OR^{5a}, -C(=O)$NR^{5a}R^a$, -C(=O)R^{5a} and optionally substituted heteroraryl

R^a is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenyl, and phenylmethyl; and wherein R^{5a} is selected from H, methyl, ethyl, isopropyl, butyl, sec-butyl, isobutyl, phenylmethyl, optionally substituted 5-6 membered heterocyclyl-C_{1-2}-alkyl, optionally substituted phenyl, and optionally substituted 5-6-membered heterocyclyl; or wherein

two R^c substituents, two R^b substituents or R^c together with R^b together form an optionally substituted fused phenyl ring; or wherein

two R^c substituents, together form an optionally substituted 3-6 membered spiro ring; in conjunction with any of the above or below embodiments.

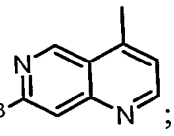
The invention also relates to compounds wherein

n is 0 or 1; in conjunction with any of the above or below embodiments;

T is O; in conjunction with any of the above or below embodiments; and

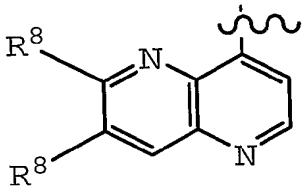
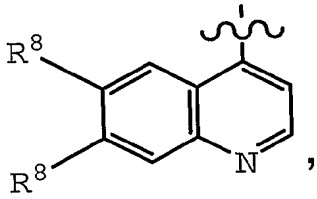
R^3 and R^4 are both H; in conjunction with any of the above or below embodiments.

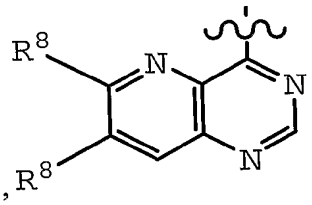
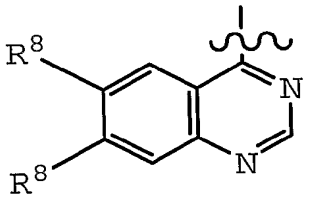
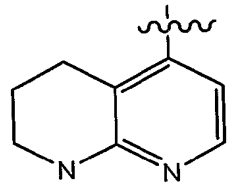
The invention also relates to compounds wherein

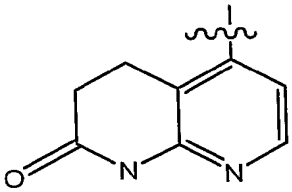
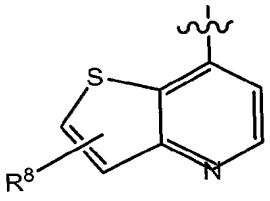
R is  ; in conjunction with any of the above or below embodiments.

The invention also relates to compounds

R is

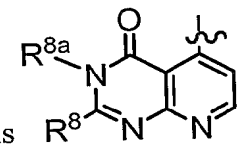
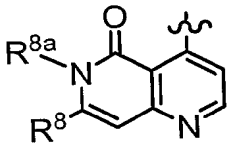
 ,  ,

 ,  ; 

 , and  ;

R^{8a} is C_{1-3} alkyl or H; in conjunction with any of the above or below embodiments.

The invention also relates to compounds wherein

R is  or  ;

R^{8a} is C_{1-3} alkyl or H ; in conjunction with any of the above or below embodiments.

The invention also relates to compounds and pharmaceutically acceptable salts and solvates thereof selected from

N-(4-(6,7-dimethoxyquinolin-4-yloxy)-3-fluorophenyl)-1-methyl-3-oxo-2-phenyl-5-(pyridin-4-yl)-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(5-(7-methoxyquinolin-4-yloxy)pyridin-2-yl)-1-methyl-3-oxo-2-phenyl-5-(pyrrolidin-1-ylmethyl)-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(4-(6,7-dimethoxyquinolin-4-yloxy)-3-fluorophenyl)-5-((ethyl(methyl)amino)methyl)-1-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide:;

N-(4-(6,7-dimethoxyquinolin-4-yloxy)-3-fluorophenyl)-5-((dimethylamino)methyl)-1-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

5-(aminomethyl)-N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-1-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

tert-butyl (4-((3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)carbamoyl)-1-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-5-yl)methylcarbamate;

N-(5-(7-methoxyquinolin-4-yloxy)pyridin-2-yl)-1-methyl-3-oxo-2-phenyl-5-(pyrrolidin-1-ylmethyl)-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-1-methyl-3-oxo-2-phenyl-5-(pyrrolidin-1-ylmethyl)-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-5-methyl-3-oxo-2-phenyl-1-((tetrahydrofuran-2-yl)methyl)-2,3-dihydro-1H-pyrazole-4-carboxamide;

5-((ethyl(methyl)amino)methyl)-N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-1-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

2-benzyl-N-(5-(7-methoxyquinolin-4-yloxy)pyridin-2-yl)-1-methyl-3-oxo-5-(pyridin-4-yl)-2,3-dihydro-1H-pyrazole-4-carboxamide;

2-benzyl-N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-1-methyl-3-oxo-5-(pyridin-4-yl)-2,3-dihydro-1H-pyrazole-4-carboxamide;

(S)-N-(5-(7-methoxyquinolin-4-yloxy)pyridin-2-yl)-1-methyl-3-oxo-2-(1-phenylethyl)-5-(pyridin-4-yl)-2,3-dihydro-1H-pyrazole-4-carboxamide;

(S)-N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-1-methyl-3-oxo-2-(1-phenylethyl)-5-(pyridin-4-yl)-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(5-(7-methoxyquinolin-4-yloxy)pyridin-2-yl)-1-methyl-3-oxo-2-phenyl-5-(pyridin-4-yl)-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-1-methyl-3-oxo-2-phenyl-5-(pyridin-4-yl)-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(5-(6,7-dimethoxyquinolin-4-yloxy)pyridin-2-yl)-1-methyl-3-oxo-2-phenyl-5-(pyridin-4-yl)-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-1-methyl-3-oxo-2-phenyl-5-(pyridin-2-yl)-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(5-(7-methoxyquinolin-4-yloxy)pyridin-2-yl)-1-methyl-3-oxo-2-phenyl-5-(pyridin-2-yl)-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-1-methyl-3-oxo-2-phenyl-5-(tetrahydro-2H-pyran-4-yl)-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(5-(7-methoxyquinolin-4-yloxy)pyridin-2-yl)-1-methyl-3-oxo-2-phenyl-5-(tetrahydro-2H-pyran-4-yl)-2,3-dihydro-1H-pyrazole-4-carboxamide;

1-Methyl-N-(5-((7-(methyloxy)-4-quinolinyl)oxy)-2-pyridinyl)-5-(2-methyl-1,3-thiazol-4-yl)-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(5-((6,7-bis(methyloxy)-4-quinolinyl)oxy)-2-pyridinyl)-1-methyl-5-(5-methyl-3-isoxazolyl)-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

1-methyl-5-(5-methyl-3-isoxazolyl)-N-(5-((7-(methyloxy)-4-quinolinyl)oxy)-2-pyridinyl)-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-((7-(methyloxy)-4-quinolinyl)oxy)phenyl)-1-methyl-5-(5-methyl-3-isoxazolyl)-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

1-methyl-N-(5-((7-(methyloxy)-4-quinolinyl)oxy)-2-pyridinyl)-3-oxo-2-phenyl-5-(2-pyrazinyl)-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-((7-(methyloxy)-4-quinolinyl)oxy)phenyl)-1-methyl-3-oxo-2-phenyl-5-(2-pyrazinyl)-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(5-((6,7-bis(methyloxy)-4-quinolinyl)oxy)-2-pyridinyl)-1-methyl-3-oxo-2-phenyl-5-(2-pyrazinyl)-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(5-((6,7-bis(methyloxy)-4-quinolinyl)oxy)-2-pyridinyl)-1-methyl-5-(2-methyl-1,3-thiazol-4-yl)-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-((7-(methyloxy)-4-quinolinyl)oxy)phenyl)-1-methyl-5-(2-methyl-1,3-thiazol-4-yl)-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(4-(6,7-dimethoxyquinolin-4-yloxy)-3-fluorophenyl)-N,1,5-trimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

2-(3-chlorophenyl)-N-(4-(6,7-dimethoxyquinolin-4-yloxy)-3-fluorophenyl)-1,5-dimethyl-3-oxo-2,3-dihydro-1H-pyrazole-4-carboxamide;

2-(3-chlorophenyl)-N-(5-(6,7-dimethoxyquinolin-4-yloxy)pyridin-2-yl)-1,5-dimethyl-3-oxo-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(4-(6,7-dimethoxyquinolin-4-yloxy)-3-fluorophenyl)-1,5-dimethyl-3-oxo-2-p-tolyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(4-(6,7-dimethoxyquinolin-4-yloxy)-3-fluorophenyl)-2-(4-fluorophenyl)-1,5-dimethyl-3-oxo-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(5-(6,7-dimethoxyquinolin-4-yloxy)pyridine-2-yl)-1,5-dimethyl-3-oxo-2-p-tolyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(5-(6,7-dimethoxyquinolin-4-yloxy)pyridin-2-yl)-2-(4-fluorophenyl)-1,5-dimethyl-3-oxo-2,3-dihydro-1H-pyrazole-4-carboxamide;

2-(3-chlorophenyl)-N-(5-(7-methoxyquinolin-4-yloxy)pyridin-2-yl)-1,5-dimethyl-3-oxo-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(5-(7-methoxyquinolin-4-yloxy)pyridin-2-yl)-1,5-dimethyl-3-oxo-2-p-tolyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

2-(2-chlorophenyl)-N-(5-(6,7-dimethoxyquinolin-4-yloxy)pyridin-2-yl)-1,5-dimethyl-3-oxo-2,3-dihydro-1H-pyrazole-4-carboxamide;

2-(2-chlorophenyl)-N-(4-(6,7-dimethoxyquinolin-4-yloxy)-3-fluorophenyl)-1,5-dimethyl-3-oxo-2,3-dihydro-1H-pyrazole-4-carboxamide;

2-(2-chlorophenyl)-N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-1,5-dimethyl-3-oxo-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-2-(4-fluorophenyl)-1,5-dimethyl-3-oxo-2,3-dihydro-1H-pyrazole-4-carboxamide;

2-(3-chlorophenyl)-N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-1,5-dimethyl-3-oxo-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(6-(6,7-dimethoxyquinolin-4-yloxy)pyridin-3-yl)-1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(2-chloro-4-(6,7-dimethoxyquinolin-4-yloxy)phenyl)-1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

2-benzyl-N-(4-(6,7-dimethoxyquinolin-4-yloxy)-3-fluorophenyl)-1,5-dimethyl-3-oxo-2,3-dihydro-1H-pyrazole-4-carboxamide;

2-benzyl-N-(5-(6,7-dimethoxyquinolin-4-yloxy)pyridin-2-yl)-1,5-dimethyl-3-oxo-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(5-(7-methoxyquinolin-4-yloxy)pyridin-2-yl)-1-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(4-(6,7-dimethoxyquinolin-4-yloxy)-3-fluorophenyl)-1-(2-hydroxy-2-methylpropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-5-methyl-3-oxo-1-(2-oxobutyl)-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-5-methyl-1-(3-methyl-2-oxobutyl)-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

(R)-N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-1-(2-hydroxybutyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-1-((2R,3R)-3-hydroxybutan-2-yl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

1-((2R,3R)-3-hydroxybutan-2-yl)-N-(5-(7-methoxyquinolin-4-yloxy)pyridin-2-yl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

(S)-1-(2-hydroxy-3-methylbutyl)-N-(5-(7-methoxyquinolin-4-yloxy)pyridin-2-yl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

(R)-1-(2-hydroxy-3-methylbutyl)-N-(5-(7-methoxyquinolin-4-yloxy)pyridin-2-yl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

(S)-N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-1-(2-hydroxy-3-methylbutyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

(R)-N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-1-(2-hydroxy-3-methylbutyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-5-methyl-1-((3-methyl-2-oxooxazolidin-5-yl)methyl)-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-1-(2-hydroxy-3-(methylamino)propyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

1-(3-chloro-2-hydroxypropyl)-N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-1-(2-hydroxy-2-methylbutyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

1-(2-hydroxy-3-methylbutyl)-N-(5-(7-methoxyquinolin-4-yloxy)pyridin-2-yl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-1-(2-hydroxy-3-methylbutyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-1-(2-hydroxy-3-morpholinopropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-5-methyl-1-(oxazolidin-5-ylmethyl)-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

(S)-N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-1-(2-hydroxybutyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

1-(3-amino-2-hydroxypropyl)-N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

1-(2-hydroxy-2-methylpropyl)-N-(5-(7-methoxyquinolin-4-yloxy)pyridin-2-yl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-1-(2-hydroxy-2-methylpropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

(R)-1-(2-hydroxypropyl)-N-(5-(7-methoxyquinolin-4-yloxy)pyridin-2-yl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

1-(3-(dimethylamino)-2-hydroxypropyl)-N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

(R)-N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-1-(2-hydroxypropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

(R)-N-(4-(6,7-dimethoxyquinolin-4-yloxy)-3-fluorophenyl)-1-(2-hydroxypropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

1-(2-hydroxypropyl)-N-(5-(7-methoxyquinolin-4-yloxy)pyridin-2-yl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(5-(6,7-dimethoxyquinolin-4-yloxy)pyridin-2-yl)-1-(2-hydroxy-2-methylpropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

(R)-2-(3-chlorophenyl)-N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-1-(2-hydroxypropyl)-5-methyl-3-oxo-2,3-dihydro-1H-pyrazole-4-carboxamide;

(R)-2-(3-chlorophenyl)-1-(2-hydroxypropyl)-N-(5-(7-methoxyquinolin-4-yloxy)pyridin-2-yl)-5-methyl-3-oxo-2,3-dihydro-1H-pyrazole-4-carboxamide;

(R)-N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-2-(4-fluorophenyl)-1-(2-hydroxypropyl)-5-methyl-3-oxo-2,3-dihydro-1H-pyrazole-4-carboxamide

1-(2-hydroxy-2-methylpropyl)-N-(5-(1-oxo-7-methoxyquinolin-4-yloxy)pyridin-2-yl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-Fluoro-4-(7-hydroxyquinolin-4-yloxy)phenyl)-1-(2-hydroxy-2-methylpropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

1-(2-hydroxy-2-methylpropyl)-N-(5-(7-hydroxyquinolin-4-yloxy)pyridin-2-yl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(4-(6-Ethyl-7-methoxyquinolin-4-yloxy)-3-fluorophenyl)-1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-Fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-(7-Methoxyquinolin-4-yloxy)phenyl)-1,2-dimethyl-3-oxo-5-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(5-(7-Methoxyquinolin-4-yloxy)pyridin-2-yl)-1,2-dimethyl-3-oxo-5-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(4-(6,7-Dimethoxyquinolin-4-yloxy)-3-fluorophenyl)-1,2-dimethyl-3-oxo-5-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(5-(7-Methoxyquinolin-4-yloxy)pyridin-2-yl)-1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

(R)-1-(2-Hydroxypropyl)-N-(5-(7-methoxyquinolin-4-yloxy)pyridin-2-yl)-2-methyl-3-oxo-5-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

(R)-N-(3-Fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-1-(2-hydroxypropyl)-2-methyl-3-oxo-5-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide

(S)-N-(3-fluoro-4-(6-methoxyquinolin-4-yloxy)phenyl)-1-(2-hydroxypropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

1-(2-aminoethyl)-N-(3-fluoro-4-((7-(methyloxy)-4-quinolinyl)oxy)phenyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide

1-(2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)ethyl)-N-(3-fluoro-4-((7-(methyloxy)-4-quinolinyl)oxy)phenyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

1-(2-aminoethyl)-N-(3-fluoro-4-((7-(methyloxy)-4-quinolinyl)oxy)phenyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

5-methyl-N-(5-((7-(methyloxy)-4-quinolinyl)oxy)-2-pyridinyl)-3-oxo-2-phenyl-1-(phenylmethyl)-2,3-dihydro-1H-pyrazole-4-carboxamide

1-benzyl-N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

5-methyl-1-(2-(methyloxy)ethyl)-N-(5-((7-(methyloxy)-4-quinolinyl)oxy)-2-pyridinyl)-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-((7-(methyloxy)-4-quinolinyl)oxy)phenyl)-5-methyl-1-(2-(methyloxy)ethyl)-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

1-(2-hydroxyethyl)-5-methyl-N-(5-((7-(methyloxy)-4-quinolinyl)oxy)-2-pyridinyl)-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

1-((2R)-2-fluoropropyl)-5-methyl-N-(5-((7-(methyloxy)-4-quinolinyl)oxy)-2-pyridinyl)-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

(S)-1-(2-(dimethylamino)propyl)-N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-((7-(methyloxy)-4-quinolinyl)oxy)phenyl)-5-methyl-3-oxo-2-phenyl-1-(2-(1-pyrrolidinyl)ethyl)-2,3-dihydro-1H-pyrazole-4-carboxamide;

1-((2S)-2-fluoropropyl)-5-methyl-N-(5-((7-(methyloxy)-4-quinolinyl)oxy)-2-pyridinyl)-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-((7-(methyloxy)-4-quinolinyl)oxy)phenyl)-1-((2S)-2-fluoropropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

1-((2S)-2-(acetylamino)propyl)-N-(3-fluoro-4-((7-(methyloxy)-4-quinolinyl)oxy)phenyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

1-((2S)-2-aminopropyl)-N-(3-fluoro-4-((7-(methyloxy)-4-quinolinyl)oxy)phenyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

1-((2S)-2-azidopropyl)-N-(3-fluoro-4-((7-(methyloxy)-4-quinolinyl)oxy)phenyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-((7-(methyloxy)-4-quinolinyl)oxy)phenyl)-1-(2-hydroxyethyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-((7-(methyloxy)-4-quinolinyl)oxy)phenyl)-5-methyl-3-oxo-2-phenyl-1-propyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(4-((6,7-bis(methyloxy)-4-quinolinyl)oxy)-3-fluorophenyl)-1-((2R)-2-hydroxypropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(4-((6,7-bis(methyloxy)-4-quinolinyl)oxy)-3-fluorophenyl)-1-((2S)-2-hydroxypropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

5-methyl-N-(5-((7-(methyloxy)-4-quinolinyl)oxy)-2-pyridinyl)-1-(2-methylpropyl)-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

5-methyl-N-(5-((7-(methyloxy)-4-quinolinyl)oxy)-2-pyridinyl)-3-oxo-2-phenyl-1-propyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-((7-(methyloxy)-4-quinolinyl)oxy)phenyl)-5-methyl-3-oxo-1-(2-oxopropyl)-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

1-(2,3-dihydroxy-2-methylpropyl)-N-(3-fluoro-4-((7-(methyloxy)-4-quinolinyl)oxy)phenyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-((7-(methyloxy)-4-quinolinyl)oxy)phenyl)-1-(2-hydroxypropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(4-((6,7-bis(methyloxy)-4-quinazolinyl)oxy)-3-fluorophenyl)-1-(2-hydroxy-2-methylpropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-((7-(methyloxy)-4-quinolinyl)oxy)phenyl)-5-methyl-1-(2-methyl-2-propen-1-yl)-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(4-((6,7-bis(methyloxy)-4-quinolinyl)oxy)-3-fluorophenyl)-1-((2S)-2-hydroxypropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(4-((6,7-bis(methyloxy)-4-quinolinyl)oxy)-3-fluorophenyl)-5-methyl-3-oxo-1-(2-oxopropyl)-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(4-((6,7-bis(methyloxy)-4-quinolinyl)oxy)-3-fluorophenyl)-1-(2,3-dihydroxy-2-methylpropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(4-((6,7-bis(methyloxy)-4-quinolinyl)oxy)-3-fluorophenyl)-5-methyl-1-(2-methyl-2-propen-1-yl)-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(5-((6,7-bis(methyloxy)-4-quinolinyl)oxy)-2-pyridinyl)-5-methyl-3-oxo-2-phenyl-1-propyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(4-((6,7-bis(methyloxy)-4-quinolinyl)oxy)-3-fluorophenyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(5-((6,7-bis(methyloxy)-4-quinolinyl)oxy)-2-pyridinyl)-5-methyl-3-oxo-2-phenyl-1-(2-propen-1-yl)-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(4-((6,7-bis(methyloxy)-1-oxido-4-quinolinyl)oxy)-3-fluorophenyl)-5-methyl-3-oxo-2-phenyl-1-(2-propen-1-yl)-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(4-((6,7-bis(methyloxy)-4-quinolinyl)oxy)-3-fluorophenyl)-5-methyl-3-oxo-2-phenyl-1-(phenylmethyl)-2,3-dihydro-1H-pyrazole-4-carboxamide;

4-(6,7-Dimethoxyquinolin-4-yloxy)-3-fluoro-N-(5-oxo-1-phenyl-2,5-dihydro-1H-pyrazol-3-yl)benzamide;

4-(6,7-Dimethoxyquinolin-4-yloxy)-N-((1,2-dimethyl-5-oxo-3-phenyl-2,5-dihydro-1H-pyrazol-4-yl)methyl)-3-fluorobenzamide;

4-(6,7-Dimethoxyquinolin-4-yloxy)-N-(2,3-dimethyl-5-oxo-1-phenyl-2,5-dihydro-1H-pyrazol-4-yl)-3-fluorobenzamide

4-(6,7-Dimethoxyquinolin-4-yloxy)-N-((2,3-dimethyl-5-oxo-1-phenyl-2,5-dihydro-1H-pyrazol-4-yl)methyl)-3-fluorobenzamide;

1-Benzyl-N-(5-(7-methoxyquinolin-4-yloxy)pyridin-2-yl)-2-oxo-1,2-dihydropyrazolo[1,5-a]pyridine-3-carboxamide;

4-((5-(6,7-Dimethoxyquinolin-4-yloxy)pyridin-2-ylamino)methyl)-1,5-dimethyl-2-phenyl-1,2-dihydropyrazol-3-one;

N-(3-fluoro-4-(2-(3-methyl-1,2,4-oxadiazol-5-yl)thieno[3,2-b]pyridin-7-yloxy)phenyl)-1-(2-hydroxy-2-methylpropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-((2-(1-methyl-1H-imidazol-5-yl)thieno[3,2-b]pyridin-7-yl)oxy)phenyl)-1-(2-hydroxy-2-methylpropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-((2-(1-methyl-1H-imidazol-5-yl)thieno[3,2-b]pyridin-7-yl)oxy)phenyl)-1-((2R)-2-hydroxypropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-(7H-pyrrolo[2,3-d]pyrimidin-4-yloxy)phenyl)-1-(2-hydroxy-2-methylpropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-(1H-pyrrolo[2,3-b]pyridin-4-yloxy)phenyl)-1-(2-hydroxy-2-methylpropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

Methyl(6-((4-(((1-(2-hydroxy-2-methylpropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)carbonyl)amino)phenyl)oxy)-1H-benzimidazol-2-yl)carbamate;

N-(4-(2-(azetidine-1-carbonyl)thieno[3,2-b]pyridin-7-yloxy)-3-fluorophenyl)-5-methyl-3-oxo-2-phenyl-1-propyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

7-(2-fluoro-4-(1-(2-hydroxy-2-methylpropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamido)phenoxy)-N-methylthieno[3,2-b]pyridine-2-carboxamide;

N-(3-fluoro-4-(2-(1-methylpiperazine-4-carbonyl)thieno[3,2-b]pyridin-7-yloxy)phenyl)-1-(2-hydroxy-2-methylpropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(2-(dimethylamino)ethyl)-7-(2-fluoro-4-(1-(2-hydroxy-2-methylpropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamido)phenoxy)thieno[3,2-b]pyridine-2-carboxamide;

N-(4-(2-(3-(dimethylamino)pyrrolidine-1-carbonyl)thieno[3,2-b]pyridin-7-yloxy)-3-fluorophenyl)-1-(2-hydroxy-2-methylpropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

7-(2-fluoro-4-(1-(2-hydroxy-2-methylpropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamido)phenoxy)-N,N-dimethylthieno[3,2-b]pyridine-2-carboxamide;

7-(2-fluoro-4-(1-(2-hydroxy-2-methylpropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamido)phenoxy)thieno[3,2-b]pyridine-2-carboxamide;

N-(2-(dimethylamino)ethyl)-7-(2-fluoro-4-(1-(2-hydroxy-2-methylpropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamido)phenoxy)-N-methylthieno[3,2-b]pyridine-2-carboxamide;

7-(2-fluoro-4-(1-(2-hydroxy-2-methylpropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamido)phenoxy)-N-(2-methoxyethyl)thieno[3,2-b]pyridine-2-carboxamide;

N-(4-(2-(azetidine-1-carbonyl)thieno[3,2-b]pyridin-7-yloxy)-3-fluorophenyl)-1-(2-hydroxy-2-methylpropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-cyclopropyl-7-(2-fluoro-4-(1-(2-hydroxy-2-methylpropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamido)phenoxy)thieno[3,2-b]pyridine-2-carboxamide

7-(2-fluoro-4-(5-methyl-3-oxo-2-phenyl-1-propyl-2,3-dihydro-1H-pyrazole-4-carboxamido)phenoxy)thieno[3,2-b]pyridine-2-carboxamide;

N-(3-fluoro-4-(6-(pyrrolidine-1-carboxamido)pyrimidin-4-yloxy)phenyl)-1-(2-hydroxy-2-methylpropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-(6-(pyrrolidine-1-carboxamido)pyrimidin-4-yloxy)phenyl)-5-methyl-3-oxo-2-phenyl-1-propyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(6-(4-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamido)-2-fluorophenoxy)pyrimidin-4-yl)morpholine-4-carboxamide;

N-(6-(2-fluoro-4-(5-methyl-3-oxo-2-phenyl-1-propyl-2,3-dihydro-1H-pyrazole-4-carboxamido)phenoxy)pyrimidin-4-yl)morpholine-4-carboxamide;

N-(6-(2-fluoro-4-(5-methyl-3-oxo-2-phenyl-1-propyl-2,3-dihydro-1H-pyrazole-4-carboxamido)phenoxy)pyrimidin-4-yl)piperidine-1-carboxamide;

N-(6-(2-fluoro-4-(5-methyl-3-oxo-2-phenyl-1-propyl-2,3-dihydro-1H-pyrazole-4-carboxamido)phenoxy)pyrimidin-4-yl)-4-methylpiperazine-1-carboxamide;

(R)-N-(4-(6-(3-(dimethylamino)pyrrolidine-1-carboxamido)pyrimidin-4-yloxy)-3-fluorophenyl)-5-methyl-3-oxo-2-phenyl-1-propyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

(R)-N-(4-(6-aminopyrimidin-4-yloxy)-3-fluorophenyl)-1-(2-hydroxypropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-(2-(pyrrolidine-1-carboxamido)pyridin-4-yloxy)phenyl)-1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(4-(4-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamido)-2-fluorophenoxy)pyridin-2-yl)piperidine-1-carboxamide;

(R)-N-(4-(2-(3-(dimethylamino)pyrrolidine-1-carboxamido)pyridin-4-yloxy)-3-fluorophenyl)-1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-(2-(pyrrolidine-1-carboxamido)pyridin-4-yloxy)phenyl)-1-(2-hydroxy-2-methylpropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-(2-(pyrrolidine-1-carboxamido)pyridin-4-yloxy)phenyl)-5-methyl-3-oxo-2-phenyl-1-propyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(4-(4-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamido)-2-fluorophenoxy)pyridin-2-yl)morpholine-4-carboxamide;

N-(4-(2-fluoro-4-(1-(2-hydroxy-2-methylpropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamido)phenoxy)pyridin-2-yl)piperidine-1-carboxamide;

5-methyl-N-(4-((7-(methyloxy)-4-quinolinyl)methyl)phenyl)-3-oxo-2-phenyl-1-propyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(4-(hydroxy(7-methoxyquinolin-4-yl)methyl)phenyl)-5-methyl-3-oxo-2-phenyl-1-propyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

1,5-dimethyl-N-(5-((7-(methyloxy)-4-quinolinyl)oxy)-2-pyrimidinyl)-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

5-methyl-N-(4-((7-(methyloxy)-4-quinolinyl)sulfinyl)phenyl)-3-oxo-2-phenyl-1-propyl-2,3-dihydro-1H-pyrazole-4-carboxamide

1-(2-hydroxy-2-methylpropyl)-5-methyl-N-(4-((7-(methyloxy)-4-quinolinyl)thio)phenyl)-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide

5-methyl-N-(4-((7-(methyloxy)-4-quinolinyl)thio)phenyl)-3-oxo-2-phenyl-1-propyl-2,3-dihydro-1H-pyrazole-4-carboxamide

5-methyl-N-(3-((7-(methyloxy)-4-quinolinyl)oxy)propyl)-3-oxo-2-phenyl-1-propyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

5-methyl-N-(trans-4-((7-(methyloxy)-4-quinolinyl)oxy)cyclohexyl)-3-oxo-2-phenyl-1-propyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

5-methyl-N-(cis-4-((7-(methyloxy)-4-quinolinyl)oxy)cyclohexyl)-3-oxo-2-phenyl-1-propyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

1-(2-hydroxy-2-methylpropyl)-5-methyl-N-(trans-4-((7-(methyloxy)-4-quinolinyl)oxy)cyclohexyl)-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide

5-methyl-N-(4-((7-(methyloxy)-4-quinolinyl)amino)phenyl)-3-oxo-2-phenyl-1-propyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

5-methyl-N-(5-((7-(methyloxy)-4-quinolinyl)oxy)-2-pyrimidinyl)-3-oxo-2-phenyl-1-propyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(3-fluoro-4-((7-(methyloxy)-4-quinolinyl)amino)phenyl)-1-(2-hydroxy-2-methylpropyl)-5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

1-(2-hydroxy-2-methylpropyl)-5-methyl-4-((7-((7-(methyloxy)-4-quinolinyl)oxy)-2,3-dihydro-4H-1,4-benzoxazin-4-yl)carbonyl)-2-phenyl-1,2-dihydro-3H-pyrazol-3-one;

1-(2-hydroxy-2-methylpropyl)-5-methyl-N-(4-((7-(methyloxy)-4-quinolinyl)amino)phenyl)-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;

N-(4-(6,7-dimethoxyquinolin-4-yloxy)-3-fluorophenyl)-3-hydroxy-2-(1-oxoisoindolin-2-yl)propanamide;

N-(4-(6,7-dimethoxyquinolin-4-yloxy)-3-fluorophenyl)-2-(1-oxoisoindolin-2-yl)acetamide;

N-(4-(6,7-dimethoxyquinolin-4-yloxy)-3-fluorophenyl)-2-oxo-1,5-diphenyl-1,2-dihydropyridine-3-carboxamide;

N-(5-((6,7-bis(methyloxy)-4-quinolinyl)oxy)-2-pyridinyl)-6-oxo-1-(phenylmethyl)-1,1',2',3',6,6'-hexahydro-3,4'-bipyridine-5-carboxamide;

N-(5-((6,7-bis(methyloxy)-4-quinolinyl)oxy)-2-pyridinyl)-6-oxo-1-(phenylmethyl)-1,6-dihydro-3,3'-bipyridine-5-carboxamide;

N-(5-((6,7-bis(methyloxy)-4-quinolinyl)oxy)-2-pyridinyl)-6'-oxo-1'-(phenylmethyl)-1',6'-dihydro-2,3'-bipyridine-5'-carboxamide

N-(5-((6,7-bis(methyloxy)-4-quinolinyl)oxy)-2-pyridinyl)-2-oxo-1-(phenylmethyl)-5-(2-thienyl)-1,2-dihydro-3-pyridinecarboxamide;

N-(5-((6,7-bis(methyloxy)-4-quinolinyl)oxy)-2-pyridinyl)-2-oxo-1-(phenylmethyl)-5-(2-pyrazinyl)-1,2-dihydro-3-pyridinecarboxamide;

N-(5-((6,7-bis(methyloxy)-4-quinolinyl)oxy)-2-pyridinyl)-5-methyl-2-oxo-1-(phenylmethyl)-1,2-dihydro-3-pyridinecarboxamide;

N-(4-((6,7-bis(methyloxy)-4-quinolinyl)oxy)-3-fluorophenyl)-5-bromo-1-(3-methylphenyl)-2-oxo-1,2-dihydro-3-pyridinecarboxamide;

N-(4-((6,7-bis(methyloxy)-4-quinolinyl)oxy)-3-fluorophenyl)-5-(1-methyl-1H-pyrazol-4-yl)-2-oxo-1-phenyl-1,2-dihydro-3-pyridinecarboxamide;

N-(3-fluoro-4-((6-(methyloxy)-7-((3-(4-morpholinyl)propyl)oxy)-4-quinolinyl)oxy)phenyl)-2-oxo-5-phenyl-1-(phenylmethyl)-1,2-dihydro-3-pyridinecarboxamide;

1,1-dimethylethyl 5-(((5-((6,7-bis(methyloxy)-4-quinolinyl)oxy)-2-pyridinyl)amino)carbonyl)-6-oxo-1-(phenylmethyl)-1,3',6,6'-tetrahydro-3,4'-bipyridine-1'(2'H)-carboxylate;

N-(4-((6,7-bis(methyloxy)-4-quinolinyl)oxy)-3-fluorophenyl)-2-oxo-1-(phenylmethyl)-5-(2-pyrimidinyl)-1,2-dihydro-3-pyridinecarboxamide;

N-(4-((6,7-bis(methyloxy)-4-quinolinyl)oxy)-3-fluorophenyl)-2-oxo-1-phenyl-5-(1H-pyrazol-4-yl)-1,2-dihydro-3-pyridinecarboxamide;

1-benzyl-5-bromo-N-(2-chloro-4-(6,7-dimethoxyquinolin-4-yloxy)phenyl)-2-oxo-1,2-dihydropyridine-3-carboxamide;

N-(5-(7-methoxyquinolin-4-yloxy)pyridin-2-yl)-2-oxo-1-phenyl-5-(pyridin-3-yl)-1,2-dihydropyridine-3-carboxamide;

N-(5-(7-methoxyquinolin-4-yloxy)pyridin-2-yl)-2-oxo-1-phenyl-5-(pyrazin-2-yl)-1,2-dihydropyridine-3-carboxamide;

.N-(5-(6,7-dimethoxyquinolin-4-yloxy)pyridin-2-yl)-2-oxo-1-phenyl-5-(pyridin-3-yl)-1,2-dihydropyridine-3-carboxamide;

N-(5-(6,7-dimethoxyquinolin-4-yloxy)pyridin-2-yl)-2-oxo-1-phenyl-5-(pyrazin-2-yl)-1,2-dihydropyridine-3-carboxamide;

N-(5-(6,7-dimethoxyquinolin-4-yloxy)pyridin-2-yl)-2-oxo-1-phenyl-5-(thiophen-2-yl)-1,2-dihydropyridine-3-carboxamide;

5-benzyl-N-(5-(6,7-dimethoxyquinolin-4-yloxy)pyridin-2-yl)-2-oxo-1-phenyl-1,2-dihydropyridine-3-carboxamide;

tert-butyl 4-(5-((5-(6,7-dimethoxyquinolin-4-yloxy)pyridin-2-yl)carbamoyl)-6-oxo-1-phenyl-1,6-dihydropyridin-3-yl)-5,6-dihydropyridine-1(2H)-carboxylate;

5-bromo-N-(2-chloro-4-(6,7-dimethoxyquinolin-4-yloxy)phenyl)-2-oxo-1-phenyl-1,2-dihydropyridine-3-carboxamide;

N-(5-(6,7-dimethoxyquinolin-4-yloxy)pyridin-2-yl)-4-(2-methoxyethylamino)-2-oxo-1-phenyl-1,2-dihydropyridine-3-carboxamide;

N-(5-(6,7-dimethoxyquinolin-4-yloxy)pyridin-2-yl)-2-oxo-1-phenyl-4-(tetrahydro-2H-pyran-4-ylamino)-1,2-dihydropyridine-3-carboxamide;

N-(5-(6,7-dimethoxyquinolin-4-yloxy)pyridin-2-yl)-2-oxo-1-phenyl-4-(phenylamino)-1,2-dihydropyridine-3-carboxamide;

N-(5-(6,7-dimethoxyquinolin-4-yloxy)pyridin-2-yl)-4-(4-methylpiperazin-1-yl)-2-oxo-1-phenyl-1,2-dihydropyridine-3-carboxamide;

N-(5-(6,7-dimethoxyquinolin-4-yloxy)pyridin-2-yl)-4-(methylamino)-2-oxo-1-phenyl-1,2-dihydropyridine-3-carboxamide;

N-(5-(6,7-dimethoxyquinolin-4-yloxy)pyridin-2-yl)-4-(dimethylamino)-2-oxo-1-phenyl-1,2-dihydropyridine-3-carboxamide;

4-(2-methoxyethylamino)-N-(5-(7-methoxyquinolin-4-yloxy)pyridin-2-yl)-2-oxo-1-phenyl-1,2-dihydropyridine-3-carboxamide;

N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-4-(2-methoxyethylamino)-2-oxo-1-phenyl-1,2-dihydropyridine-3-carboxamide

N-(4-((6,7-bis(methyloxy)-4-quinolinyl)oxy)-3-fluorophenyl)-1-cyclopentyl-6-oxo-5-(2-oxo-1-pyrrolidinyl)-1,6-dihydro-3-pyridinecarboxamide;

1-benzyl-N-(5-(6,7-dimethoxyquinolin-4-yloxy)pyridin-2-yl)-4-(2-methoxyethylamino)-2-oxo-1,2-dihydropyridine-3-carboxamide;

1-benzyl-N-(5-(6,7-dimethoxyquinolin-4-yloxy)pyridin-2-yl)-4-(dimethylamino)-2-oxo-1,2-dihydropyridine-3-carboxamide;

1-benzyl-N-(5-(6,7-dimethoxyquinolin-4-yloxy)pyridin-2-yl)-4-(methylamino)-2-oxo-1,2-dihydropyridine-3-carboxamide;

1-benzyl-N-(5-(6,7-dimethoxyquinolin-4-yloxy)pyridin-2-yl)-2-oxo-4-(phenylamino)-1,2-dihydropyridine-3-carboxamide;

1-benzyl-N-(5-(6,7-dimethoxyquinolin-4-yloxy)pyridin-2-yl)-2-oxo-4-(pyridin-4-ylamino)-1,2-dihydropyridine-3-carboxamide;

1-benzyl-N-(5-(6,7-dimethoxyquinolin-4-yloxy)pyridin-2-yl)-4-(4-methylpiperazin-1-yl)-2-oxo-1,2-dihydropyridine-3-carboxamide;

1-benzyl-N-(5-(6,7-dimethoxyquinolin-4-yloxy)pyridin-2-yl)-2-oxo-4-(tetrahydro-2H-pyran-4-ylamino)-1,2-dihydropyridine-3-carboxamide;

1-benzyl-N-(5-(6,7-dimethoxyquinolin-4-yloxy)pyridin-2-yl)-2-oxo-4-(4-(trifluoromethyl)phenylamino)-1,2-dihydropyridine-3-carboxamide;

1-cyclopentyl-N-(4-(6,7-dimethoxyquinolin-4-yloxy)-3-fluorophenyl)-6-oxo-5-(2-oxopyrrolidin-1-yl)-1,6-dihydropyridine-3-carboxamide;

N-(3-fluoro-4-(2-(pyrrolidine-1-carboxamido)pyridin-4-yloxy)phenyl)-3-oxo-2-phenyl-2,3-dihydropyridazine-4-carboxamide;

6-((diethylamino)methyl)-N-(4-(6,7-dimethoxyquinolin-4-yloxy)-3-fluorophenyl)-3-oxo-2-phenyl-2,3-dihydropyridazine-4-carboxamide;

6-((dimethylamino)methyl)-N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-3-oxo-2-phenyl-2,3-dihydropyridazine-4-carboxamide;

N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-6-methyl-3-oxo-2-phenyl-2,3-dihydropyridazine-4-carboxamide;

N-(5-(6,7-dimethoxyquinolin-4-yloxy)pyridin-2-yl)-6-methyl-3-oxo-2-phenyl-2,3-dihydropyridazine-4-carboxamide;

2-benzyl-N-(5-(6,7-dimethoxyquinolin-4-yloxy)pyridin-2-yl)-6-methyl-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(3-fluoro-4-(7-methoxyquinolin-4-yloxy)phenyl)-3-oxo-2-phenyl-2,3-dihydropyridazine-4-carboxamide;

N-(2-chloro-4-(6,7-dimethoxyquinolin-4-yloxy)phenyl)-6-methyl-3-oxo-2-phenyl-2,3-dihydropyridazine-4-carboxamide;

(R)-N-(4-(6,7-dimethoxyquinolin-4-yloxy)-3-fluorophenyl)-6-((3-(dimethylamino)pyrrolidin-1-yl)methyl)-3-oxo-2-phenyl-2,3-dihydropyridazine-4-carboxamide;